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Central Determinants of Attention and Mood Disorder in Tardive Dyskinesia ("Tardive Dysmentia")

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The typical apathetic state of tardive dyskinesia patients may be punctuated by periods of hyperactivity, vigilance, and tension. Patients may exhibit unusual readiness for contact, even though they remain edgy, loud and loquacious, euphoric, jolly, intrusive, and invasive of the privacy of others. These features designated as "tardive dysmentia" are examined, so as to draw attention to the possibility that the syndrome of dysmentia is comprised of occasional excessive emotional reactivity, enhanced responsiveness to environmental stimuli, and indifference to or reduced awareness of the patient's abnormal involuntary movements. The pathophysiology of tardive dysmentia remains uncertain. It is proposed that behavioral changes in patients with dysmentia may be conceived in terms of a more outward direction of attentional processing. Such an immense change in psychopathology under antipsychotic drugs, from withdrawal to the emotional externalization of behavior, is conceived as reflecting a shift in the approach–avoidance behavior due to alterations in the parieto-frontal balance.

The interest in an interaction between cognition and movement traces its ancestry to Sechenov's famous dictum that "all the endless diversity of the external manifestations of the brain can finally be regarded as one phenomenon—that of muscular movement" (Sechenov, 1893). The communality between motion and cognitive effort is frequently emphasized by pointing at the parallelism of their disintegration in disorders of movement (e.g., parkinsonism, Huntington's chorea). Tardive dyskinesia (TD) represents yet another disorder to test the issue, but the question of what kind of impairment of cognition, if any, is contributed by TD still eludes our grasp.

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DEFINING THE ISSUE

Signs of neurological deficit in the form of structural abnormalities in the basal ganglia, enlarged ventricles, and sulcal markings is a common finding in patients with TD (Christensen, Moller, & Faurbye, 1970; Bartels & Themelis, 1983). There is an excessive number of left-handers among TD patients (Joseph, 1990). Dyskinetic patients with a secondary diagnosis of organic brain syndrome have a higher degree of severity of TD symptoms (Chouinard, Annable, Ross-Chouinard, & Nestoros, 1979; Fleischhauer, Kocher, Hobi, & Gilsdorf, 1985). This neurological background is likely to increase with advancing years. A deficit of cognition in TD, too, is commonly seen in the elderly and/or organically impaired individuals (Waddington, 1987). Given that most cognitive studies in TD are cross-sectional, we cannot rule out that cognitively disadvantaged patients are recruited from a population that was impaired prior to receiving neuroleptic medication. TD may occur in young patients, nonpsychotic subjects, and non-brain-damaged patients who are receiving chronic neuroleptic treatment (Klawans, Bergen, Bruyn, et al., 1974). One might therefore legitimately ask whether TD, developing in young patients, would lead to a cognitive breakdown? To answer this question, Collerton, Fairbairn, and Britton (1985) selected dyskinetic patients with no significant atrophy of brain tissue and instructed them to execute cued responses in a novel cognitive task. Their patients performed comparable to the nondyskinetic controls in this paradigm. Gold, Egan, Goldberg, and Kirch (1989) examined their group of age-matched TD patients on the WAIS-R and Halstead–Reitan batteries. They found a meager evidence of clinically significant cognitive impairment in dyskinesia. Predictably, however, it was obtained in older patients. Thus TD can be—which is not the same as saying must be—associated with cognitive impairment (e.g., Kolakowska, Williams, Ardern, & Revely, 1986; Richardson, Pass, Bregman, & Craig, 1986; Wolf, Ryan, & Mosnaim, 1983). The TD patients studied by Collerton et al. (1985) even manifested signs of cognitive facilitation. The finding of their superior cued performance in the latter study is of interest if we recall that speed of functioning and, notably, cognitive speed, is a more vulnerable function and is more impaired than the level of intellectual functioning in schizophrenia (Nelson, Pantelis, Carruthers, Speller, Baxendale, & Barnes, 1990).

There is still another possibility that patients' cognitive efforts vary as a function of their motivation and vigilance. The typical apathetic state of TD patients may be punctuated by periods of hyperactivity, vigilance, and tension. Patients may exhibit unusual readiness for contact, even though they remain edgy, loud and loquacious, euphoric, jolly, intrusive, and invasive of the privacy of others (Myslobodsky, 1986). This paradoxical combination of apathy, irritability, and euphoria is suggestive of a

frontal lobe deficit (Geschwind, 1977). However, such soaring or plummeting of mood in TD has rarely been studied. We therefore focus our discussion on these concomitant signs and their relevance to genesis of cognitive disturbances.

THE TRIAD OF TARDIVE DYSMENTIA

Wilson, Garbutt, Lanier, Moylan, Nelson, and Prange (1983) hypothesized that the pattern of approach behavior coupled with edginess and excessive affect represent a new, neuroleptic-induced syndrome designated as "tardive dysmentia." Its prevalence remains unknown since these signs may not appear as a pure and lasting syndrome. However, they are not discordant intrusions. Chard, Sharon, and Myslobodsky (1986) compared nine TD patients with a mean Abnormal Involuntary Movement Scale (Guy, 1976) rating of 2 or more and no detectable signs of neurological damage with six non-TD patients matched for age and education. All were under 45 years of age (TD patients were 39.7 ± 5.72 and nondyskinetic patients were 36.8 ± 6.49 years old). None of them showed signs of dementia on the Mini-Mental State Examination (Folstein, Folstein, & McHugh, 1975). Table 1 summarizes the profile of this sample on the Multiple Affect Adjective Check List (MAACL) (Zuckerman & Lubin, 1965) validated for the Hebrew-speaking population (Chard, 1985). It shows that the TD group scored somewhat higher on practically all items of the MAACL, with significant difference on the aggression and tension items. We noted that patients' complaints and edginess occurred against a background of a marginally significant score of euphoria (Table 1). This is of some interest for two reasons: first, neuroleptics are widely believed to cause chiefly dysphoric or depressive states (McGlashan & Carpenter, 1976; Singh & Kay, 1979), and second, TD patients are reported to show a higher incidence of negative symptoms (Waddington, 1987).

TABLE 1
The Comparison of Schizophrenic Patients with and without TD on Affect Variable of the MAACL and Cantril's Score

Affect variable	TD group	non-TD group	$t(df = 13)$	$p<$
		MACCL scale		
Depression	9.77 ± 7.22	6.57 ± 6.05	.654	ns
Positive affect	22.00 ± 3.46	15.57 ± 8.96	1.985	.07
Elation	9.11 ± 4.56	6.14 ± 3.97	1.357	ns
Agression	5.50 ± 4.11	.42 ± .58	3.195	.01
Tension	4.33 ± 2.87	.57 ± .98	3.298	.005
Cantril's score	7.22 ± 3.23	6.85 ± 3.33	.221	ns

Apparently, anosognosia is one of the more permanent signs of TD (Myslobodsky, 1986). Although Tarsy (1983) reported that failure to complain of severe dyskinesia is more common for demented institutionalized patients, the present study does not support this observation. Anosognosia is ubiquitous in the elderly, indeed, but may be easily seen among younger, cognitively unimpaired dyskinetic patients. Six of nine TD patients examined by Chard et al. (1986) were completely indifferent to their dyskinesia. Note that anosognosia by and large represents the lack of awareness of the "negative" symptom such as blindness, hemianopsia, hemineglect, or hemiplegia. In contrast, TD patients appeared to be startlingly oblivious of the grotesque "positive" signs. This lacunar self-observation was not due to a general reduction of awareness. TD patients may often be found trailing behind doctors or nurses with a number of somatic complaints, but not about their motor disturbances. To paraphrase from Rechtschaffen (1978) their "motor awareness" may be isolated from other systems of consciousness; or rather, TD patients lose the motor part of their "road map of consciousness."

Another peculiar feature of dysmentia is the stimulus boundness of TD patients. It may be compared to that of demented patients who show signs of environmental dependency: they tend to move objects during an interview and incessantly trail behind people (Fairburn & Hope, 1988). Three patients of the TD group presented in Table 1 constantly attempted to touch others. Their manual reaching was reminiscent of akathisia in its persistence, or rather, compulsions without inner restlessness, anxiety, or guilt of the latter condition. They also denied having touched other patients. It is of interest that two of these patients had the grasp and palmomental reflexes that are considered to be "frontal lobes signs" (Geschwind, 1977). In summary, the features of dysmentia in TD may be summarized as a triad of symptoms: occasional excessive emotional reactivity, enhanced responsiveness to environmental stimuli, and indifference or reduced awareness of abnormal involuntary movements.

Why are these features so special? Although TD is seen *not* only in schizophrenic patients, most TD patients discussed here were diagnosed as having schizophrenia. Ever since Kraepelin (1919), the schizophrenic is described as being idle, with reduced drives and shallow expression of emotions. This state is likely only to worsen with aging (Miller & Cohen, 1987) for the patients with positive symptoms are also known to develop negative symptoms as schizophrenia progresses (Crow, 1988). Even those who occasionally manifest multiple affective states remain immobilized and impotent, torn by contradictory impulses. They tend to preserve themselves by retreating into the realm of existence with thought and behaviors that have a most private code. This codification of thoughts was designated by Bleuler (1950) as being "autistic." Among more recent writers, Ey (1959, 1978) consistently conceived of schizophrenia as a

process of retreat or gradual *withdrawal,* as a "rupture of existential communications and fall into an imaginary world" (p. 708) . . . that "leads to a progressively closed form of existence" (Ey, 1959; p. 710). The recovery from apathy after neuroleptic treatment complicated by dyskinesia might seem striking inasmuch as a patient becomes more reachable and open in expression of pleasure and distress. Some patients with TD may be likened to the manic who according to Kraepelin (1919) "seeks relations with his surroundings" (p. 268). Therefore, we believe that the implied purpose of giving the name of tardive dysmentia (Wilson et al., 1983) may be justified even if only to emphasize the immense change of psychopathology under antipsychotic drugs, from autism to the emotional externalization of behavior.

WHAT CAUSES DYSMENTIA TO EVOLVE?

Dysmentia may be misdiagnosed. Schizoaffective patients and/or frank manic-depressives are known to be often misdiagnosed as schizophrenics (Kety, 1985). Individuals with affective and schizoaffective psychoses seem to be prone to develop TD (Kane, Woerner, & Lieberman, 1985). Affective tension and enhanced vigilance increase the intensity of TD and are believed to affect the rate of its prevalence (Fleischhauer et al., 1985). Clinical findings suggest that hyperactivity of central dopaminergic pathways may be an important component of the pathophysiology of manic states (Murphy, Brodie, Goodwin, & Bunney, 1971). Wilson et al. (1983) mentioned, however, that their patients with tardive dysmentia were presented originally as typical schizophrenics with reduced volition, autistic preoccupation, social withdrawal, and impoverished affect. Mukherjee (1984) also observed no case of behavior characteristic of dysmentia in patients with affective psychosis complicated by TD due to long-term neuroleptic exposure.

Another possibility is that the evolution into dysmentia is associated with anticholinergic medication. The reason for this attribution stems from a noticeable change in mood when anticholinergic treatment in TD patients is discontinued. They soon reverse to immobile, withdrawn, unhappy patients, who complain of increased rigidity (Myslobodsky, Holden, & Sandler, 1985a; Myslobodsky, Tomer, Holden, Kempler, & Sigal, 1985b), as though abnormal involuntary movements ("loosening the limbs") have acted as rewarding stimuli (Miller, Wickens, & Benninger, 1984).

A third, more viable alternative might be to attribute these TD symptoms in schizophrenic patients to excessive stimulation of neurotransmitter systems underlying motivation and reward. It can be assumed that TD is associated with an apparent relative dopaminergic, and possibly norepinephrinergic, overactivity (e.g., Jeste and Wyatt, 1982). Both systems are implicated in a number of reinforcing states. The dopaminergic circuits are believed to act as an intermediary between the motor and limbic systems. They govern attention to stimuli that have motivational salience, and thereby control the achievement of external rewards in the context of species-specific "foraging" tendencies (Panksepp, 1982). Wise (1982) suggests that dopamine impairment primarily disrupts motivational arousal to external rather than to internal stimuli: "it is attention to *environmental* stimuli that would normally have motivational salience that is lost under neuroleptic treatment" (p. 52) (italics added). The change in emotional behavior consequent to TD may thus be attributed to the rebound dopaminergic activity that contributes to motivational arousal with enhanced hedonic impact of reward, heightened vigilance, and affective tension.

TARDIVE DYSMENTIA: THE SYNDROME OF ENVIRONMENTAL DEPENDENCY?

The terms, "stimulus boundness" and "environmental dependency syndrome" were coined by Lhermitte, Pillon, and Serdaru (1986). They noted that frontal lobe patients manifest an unusual dependence upon social and physical environmental cues. These patients also tend to imitate gestures of the examiner, and manipulate any physical objects within their reach, even though these objects are completely irrelevant to social circumstances. These "imitation" and "utilization behaviors" were conceived as the "environmental dependency syndrome," in which patients behaved as "though implicit in the environment was an order to respond to the situation in which they found themselves" (Lhermitte, 1986). Interpreting these findings into a theory, Lhermitte proposes this bizarre behavior to be a result of activity of the parietal cortex unopposed by the prefrontal inhibitory circuits. The notion of mutual fronto-parietal inhibitory connections was well appreciated by Denny-Brown and Chambers (1958) who linked positive (in neurological, i.e., Jacksonian terms) aspects of behavior to frontal lobe disease and negative behaviors to parietal deficit. Such motor phenomena as withdrawal of a hand from any new stimulus or such phenomena as extinction in patients with parietal lesions were interpreted as "avoiding reaction" and/or negative aspects of behavior. In contrast, a "magnet" or an exploration of space by the affected hand were designated as the tonic or "forced grasp reflex" representing positive symptoms associated with frontal lobe lesion. Lhermitte's environmental dependency syndrome appeared to be a significant support of Denny-Brown's concept whose impact was to refocus attention upon the psychopathological implications of the disorder. Mesulam (1986) proposed that the syndrome of hemineglect in patients with parietal lesion may be conceived as some sort of psychological withdrawal, an opposite of the environmental dependency syndrome.

Excessive psychomotor impulse created by a shift of the "fronto-parietal seesaw" may be especially compelling on a background of the enhanced motivational arousal in TD, facilitating the so-called stimulus-bound behavior (Valenstein, 1971). Using a rat as an experimental animal, Valenstein (1971) showed that stimulus-specific patterns of behavior could be determined by the goal–object available in the cage when general enhancement of arousal and motivation has been created by electrical stimulation delivered to a broad area of the hypothalamus and even outside of it. Thus, in the presence of previously indifferent stimuli, an aroused animal would exhibit signs of environmental dependency by responding to any of them in an object-specific way (feeding, copulation, drinking, carrying objects, etc.). Likewise, the patterns exemplified by Lhermitte (1986) can be easily switched from one type of response to another with no apparent aftereffect from the previous behavior. Various features of the environment dependency syndrome were exhibited only during the period of "stimulation," such as seeing a gesture produced by the examiner or an object displayed in the office. From the fact that a patient conducted a new and highly specific act, a learning theorist could hypothesize an enhanced arousal that activated a motivational state and channeled behavior to an otherwise indifferent stimulus.[1]

Could cognitive deficits in TD reflect a change in the fronto-parietal balance? The answer could be in the affirmative. It has long been noticed that patients with parietal lesions fail to learn sequential manual and leg movements. Similar sequences may be reproduced, however awkwardly, by patients with precentral lesions (Kaidanova & Meierson, 1964, cited in Tonkonogi, 1973). Tonkonogi (1973) argues that this deficit represents a form of apraxia for new complex movements. Similar findings were obtained by Kimura (1977, 1982) and later supported by Kolb & Milner (1981). The latter examined patients after unilateral brain operation with removals from the left or right frontal, central, parietal, temporal, and occipital areas. Comparing the tasks requiring imitation of a series of oro-facial movements vs. manual sequences, they found that facial tasks were poorly performed following lesions of the frontal lobe of either side. In contrast, a significant impairment of the manual tasks followed left parietal area lesions. Lhermitte et al.(1986) assessed imitation of gestures in a less structured setting than is created in a typical neuropsychological study. Yet they arrived at a similar conclusion. None of their 75 patients with frontal-lobe syndrome ever forgot a detail of gestural sequence. One

[1] The fronto-parietal balance may be a part of a more complex system of extensive reciprocal connections between the cortical areas and the limbic structures, notably the septum. The latter is involved in monitoring the availability of exteroceptive information as it is translated in motivated behaviors along the approach–withdrawal continuum (Hermann & Lubar, 1975).

should add parenthetically that none of them had clinical disturbances implicating the temporo-parietal area.

In view of the foregoing, Myslobodsky et al. (1985b) examined an imitation of manual sequences in TD patients, using the abbreviated version of the test devised by Kimura and Archibald (1974). The TD group performed better (but not significantly so) than the non-TD controls. In contrast, the scores for the oro-facial sequences were virtually identical in both groups (Myslobodsky et al., 1985b). This finding was consistent with observations by Benson and Stuss (1982) that schizophrenic patients with prefrontal lobotomy showed no reduced competence in the imitation of three-step manual sequences compared to nonoperated patients.

More recently, Goldberg, Myslobodsky, and Weinberger (1987) used a similar test in a group of 15 non-TD schizophrenic patients and 15 normal individuals matched for age, sex, and educational level. This group was much younger compared to patients examined earlier (under 40 years compared to 62 years of age). Contrary to the above findings, patients proved less capable of imitating three-step manual sequences, but not oral sequences. A 2 × 2 analysis of variance (Groups × Tests) showed a significant main effect of diagnostic group [$F(1, 28) = 11.01$; $p < .003$] and tests [$F(1, 28) = 48.84$; $p < .001$], and significant interaction between the two [$F(1, 28) = 4.94$; $p < .05$]. What made the patients' disability even more remarkable was that those who received top scores for facial sequences were still capable of only crude approximation of three-step manual sequences.[2] What could have contributed to such a striking difference in patient performance, the age difference between the groups, the accompanying dyskinesia, or both?

HYPOFRONTALITY VS. HYPOPARIETALITY AS A CONFOUNDING VARIABLE IN TD

A likely answer is that we deal with a failure to replicate our previous results. However, with the advantage of hindsight, an interpretation we favor is that the two studies may be conceived as existing on a continuum from relatively early stages of schizophrenia to a stage when lasting medication caused a state bordering on TD. Assuming that a similar result would be obtained in a longitudinal study, one might entertain the possibility of a rostral–caudal shift of the site of deficit in schizophrenia as

[2] Heilman and Valenstein (1979) hypothesized that it is possible to distinguish between dysfunction caused by parietal lesion and that associated with the disconnection of the parietal area from motor association areas. They reasoned that patients with destroyed visuo-kinetic motor engrams in the parietal area should not recognize their disability, whereas patients with parieto-frontal disconnection should. It is of interest that some schizophrenic patients were noticeably surprised by their inadequacy in the manual task, asking for explanations of their failure or even tried to rationalize it.

indexed by Kimura's tests. That is, the younger and/or less medicated patients would be more likely to manifest some signs of the parietal syndrome, whereas the symptoms of prefrontal deficit would become increasingly noticeable with advancing years and lasting neuroleptic medication. This prediction needs to be tested in a longitudinal study. Yet, while this report was being prepared, Zimmerman and Hermesh (1991) examined an imitation of manual and oral sequences in eight first-admission nonmedicated schizophrenic patients. Ten nondyskinetic schizophrenic patients who were on antipsychotic drugs for at least 5 years and 10 normal individuals were matched for age, handedness, education and socioeconomic level to serve as controls. Overall, all patients performed significantly worse than normal individuals on both manual sequences and facial grimaces. Yet, nonmedicated patients did somewhat better on oro-facial sequences compared to medicated patients. In contrast, the latter showed higher scores of manual sequences, albeit not high enough to match the control scores. These data reinforce the possibility that alterations of the fronto-parietal balance may occur in the course of medication and do not require the expression of TD.

Similar conclusions could be derived from studies examining regional cerebral blood flow and/or brain utilization of glucose. Both techniques initially showed a distinct reduction of frontal activity in schizophrenia which has become known as "hypofrontality" (Ingvar, 1980; Franzen & Ingvar, 1975). As the proponents of hypofrontality pressed their case (e.g., Buchsbaum, Ingvar, Kessler, et al., 1982; Wolkin, Jaeger, Brodie, et al., 1985), it has become increasingly apparent that a decreased rate of glucose utilization is more often seen in patients who for years were on neuroleptic medication. When a younger population was examined, hypofrontality was not confirmed (Mathew, Duncan, Weinman, & Bar, 1982; Mathew, Meyer, Frances, Schoolar, Weinman, & Mortel, 1981; Sheppard, Manchanda, Gruzelier, et al., 1983; Widen, Bergstrom, Blomquist, et al. 1983; Uchino, Nakane, Ohta, Hirota, Yonekura, & Mori, 1987). Mathew et al. (1981, 1982) even occasionally noticed relative hyperfrontality. In a more recent study, Szechtman, Nahmias, Garnett, Firnau, Brown, Kaplan, and Cleghorn (1988) specifically examined whether the duration of treatment with antipsychotic drugs influences the regional distribution of glucose metabolism in schizophrenia. One group of their patients was examined before medication and after a year on medication. Another group, on antipsychotic drugs 4 years or longer, was also examined. Compared with normals, metabolic tone in the former group was rather enhanced frontally. One year of medication affected very little the cortical distribution of glucose. Following 4–14 years of medication this enhanced frontal metabolic tone began to return to control values (Szechtman et al., 1988). Kishimoto, Kuwahara, Ohro, Takazu, Nakano et al. (1987) who conducted [^{11}C]glucose positron emission tomography in 27 schizophrenic patients noted hypofrontality similar to that observed with the ^{18}F-labeled deoxyglucose method (Buchsbaum et al., 1982) in only one third of their patients. In another third, a "hypoparietal" rather than a hypofrontal metabolic landscape was obtained.

Thus, it is likely that hypoparietality or hyperfrontality may be just a snapshot in a chronicle of a gradual change in the fronto-parietal balance, which may be a function of the clinical pattern of the disorder, its duration, length of neuroleptic medication, age, sex, etc. Since TD is more likely to develop on the "hypofrontal" level of such a balance, its cognitive makeup may, too, be determined by numerous variables that have to be considered when assembling a control group of nondyskinetic patients.

The parietal lobes are not considered an essential component of the TD syndrome. However, there is no reason why the parietal lobe should not be conceived in the pathophysiology of disorders caused by lasting neuroleptic medication. Students of epilepsy might recall that consistent with Mesulam's (1986) argument, parietal lobe epileptic foci can be easily camouflaged by features of the frontal lobe syndrome (Ajmone-Marsan & Goldhammer, 1973). The existence of dopaminergic projections to the posterior regions was reported for rats (Saldate & Orrego, 1977), cats (Tork & Turner, 1981), and monkeys (Lewis, Morrison, & Goldstein, 1988). The resemblance of clinical features of the malfunctioning parietal lobe to *positive* symptoms in schizophrenia is frequently so staggering that Zac and Weinberger (1986) recommend that "serious consideration should be given to this region in future investigations" (p. 192). It may, thus, be possible that some signs of "prefrontal deficit" are of parietal origin. A longitudinal study of the symptomatology accompanying TD should aid in the reconstruction of the context in which the claim could be validated.

SUMMARY

The nature of tardive dyskinesia remains uncertain. The possibility that its signs represent, so to speak, "larval dementia" is difficult to rule out (Myslobodsky, 1986). The fact that similar mood disorders are encountered in patients with frontal lobe deficit and that some patients with dysmentia manifest typical frontal lobes signs (e.g., the grasp and palmomental reflexes) is consistent with such a possibility. Yet, as often happens with the prefrontal syndrome, a patient may not appear demonstrably deficient when assessed in the neuropsychological setting. The problem is that the patient's cognitive resources and social knowledge are not implemented in the repertoires required by real life (Damasio, 1985). The magnitude and latitude of deficits in TD may require a neuroethological style of research, akin to that adopted by Lhermitte. This admonition is taken a step further in suggesting that neurochemical and

behavioral deficits in TD are not an endpoint of a process but a series of snapshots in a continuum of changes. The pathophysiological advantage of such a dimensional (longitudinal), over the categorical (cross-sectional), approach is in viewing the shift in the approach–avoidance behavior of a patient with tardive dysmentia through alterations of the parieto-frontal balance. Cognitive changes in patients with dysmentia may be conceived in terms of a more outward direction of attentional processing that could at times look as a benefit compared to the state of non-TD patients, notably those with schizophrenia, rather than the expression of alterations of some "specific functions." Direct evident is required in order to make connections between cognitive changes in TD and disorders of mood and behavior.

REFERENCES

Ajmone-Marsan, C., & Goldhammer, L. 1973. Clinical ictal patterns and electrographic data in cases of parietal seizures of fronto-central origin. In M. A. Brazier (Ed.), *Epilepsy: Its phenomena in man*. New York: Academic Press. Pp. 235–258.

Bartels, M., & Themelis, J. 1983. Computerized tomography in tardive dyskinesia. Evidence of structural abnormalities in the basal ganglia. *Archives of Psychiatry and Neurology*, **233**, 371–379.

Benson, D. F., & Stuss, D. T. 1982. Motor abilities after frontal leukotomy. *Neurology*, **32**, 1352–1357.

Bleuler, E. 1950. *Dementia praecox or the group of schizophrenias*. [Translated by J. Zinkin from the 1911 German Edition]. New York: International Univ. Press.

Brown, S. L. 1981. Dissociation of pleasure in psychopathology. *Journal of Nervous and Mental Disease*, **169**, 3–17.

Buchsbaum, M. S., Ingvar, D., Kessler, R., et al. 1982. Cerebral glucography with positron emission tomography. *Archives of General Psychiatry*, **39**, 251–259.

Cantril, H. 1965. *The pattern of human concerns*. News Brunswick, NJ: Rutgers Univ. Press.

Chard, F. 1985. *Development of a Hebrew version of the multiple adjective checklist*. MA Thesis, Tel-Aviv Univ.

Chard, F., Sharon, D., & Myslobodsky, M. S. 1986. *Anosognosia and disturbances of emotions in TD patients*. Unpublished manuscript.

Chouinard, G., Annable, L., Ross-Chouinard, A., & Nestoros, J. N. 1979. Factors related to tardive dyskinesia. *American Journal of Psychiatry*, **136**, 79–83.

Christensen, E., Moller, J. E., & Faurbye, A. 1970. Neuropathological investigations of 28 brains from patients with dyskinesia. *Acta Psychiatrica Scandinavica*, **46**, 14–23.

Collerton, D., Fairbairn, A., & Britton, P. 1985. Cognitive performance of medicated schizophrenics with tardive dyskinesia. *Psychological Medicine*, **15**, 311–315.

Crow, T. J. 1988. The two-syndrome concept: Origin and current status. *Schizophrenia Bulletin*, **11**, 578–583.

Damasio, A. 1985. The frontal lobes. In K. M. Heilman & E. Valenstein (Eds.), *Clinical neuropsychology*. New York: Oxford Univ. Press. Pp. 339–376.

Denny-Brown, D. & Chambers, R. A. 1958. The parietal lobe and behavior. *The Association for Research on Nervous and Mental Diseases*, **36**, 35–117.

Ey, H. 1959. Unity and diversity of schizophrenia: Clinical and logical analysis of the concept of schizophrenia. *American Journal of Psychology*, **115**, 706–714.

Ey, H. 1978. *Consciousness. A phenomenological study of being conscious and becoming conscious*. Bloomington: Indiana Univ. Press.

Fairburn, C. G., & Hope, R. A. 1988. Changes in behaviour in dementia: A neglected research area. *British Journal of Psychiatry*, **52**, 406–407.

Fleischhauer, J., Kocher, R., Hobi, V., & Gilsdorf, U. 1985. Prevalence of tardive dyskinesia in a clinical population. In D. E. Casey, T. N. Chase, & J. Gerlach (Eds.), *Dyskinesia: Research and treatment*. Berlin: Springer-Verlag. Pp. 162–177.

Folstein, M. F., Folstein, S. E., & McHugh, P. R. 1975. Mini-mental state: A practical method for grading the cognitive state of patients for clinicians. *Journal of Psychiatry Research*, **12**, 189–198.

Franzen, G., & Ingvar, D. H. 1975. Abnormal distribution of cerebral activity in chronic schizophrenia. *Journal of Psychiatric Research*, **12**, 199–214.

Geschwind, N. 1977. *Lectures in neurobehavior*. Boston: Harvard Univ. School of Medicine.

Gold, J., Egan, M., Goldberg, T., & Kirch, D. 1989. Cognitive impairment and tardive dyskinesia. *Schizophrenia Research*, **2**, 236P.

Goldberg, T., Myslobodsky, M. S., & Weinberger, D. 1987. *Dyspraxia of imitative manual sequences in schizophrenia*. Unpublished manuscript.

Guy, W. 1976. *ECDEU assessment manual for psychopharmacology*. US Department of Health, Education and Welfare. Revised 1976, pp. 534–537.

Heilman, K., & Valenstein, E. Eds. 1979. *Clinical neuropsychology*. New York: Oxford Univ. Press. P. 174.

Hermann, T. E., & Lubar, J. F. 1975. Immediate and long-term effects of septal and frontal ablations of the species-typical behavior of the rat. In J. F. DeFrance (Ed.), *The septal nuclei*. New York: Plenum Press. Pp. 3–35.

Ingvar, D. H. 1980. Abnormal distribution of cerebral activity in chronic schizophrenia: A neurophysiological interpretation. In C. Baxter & T. Melnechuk (Eds.), *Perspectives in schizophrenia research*. New York: Raven Press. Pp. 107–130.

Jeste, D. V., Linnoila, M., Fordis, C. M., Phelps, B. H., Wagner, R. L., & Wyatt, R. J. 1982. Enzyme studies in tardive dyskinesia. III. Noradrenergic hyperactivity in a subgroup of dyskinetic patients. *Journal of Clinical Psychopharmacology*, **2**, 318–320.

Jeste, D. V., & Wyatt, R. J. 1982. *The understanding and treating of tardive dyskinesia*. New York: The Guilford Press.

Joseph, A. B. 1990. Non-right-handedness and maleness correlate with tardive dyskinesia among patients taking neuroleptics. *Acta Psychiatrica Scandinavica*, **81**, 530–533.

Kane, J. M., Woerner, M., & Lieberman, J. 1985. Tardive dyskinesia: Prevalence, incidence, and risk factors. In D. E. Casey, T. N. Chase, & J. Gerlach (Eds.), *Dyskinesia: Research and treatment*. Berlin: Springer-Verlag. Pp. 72–77.

Kety, S. S. 1985. The concept of schizophrenia. In M. Alpert (Ed.), *Controversies in schizophrenia*. New York: The Guilford Press. Pp. 3–11.

Kimura, D. 1977. Acquisition of motor skill after left-hemisphere damage. *Brain*, **100**, 527–542.

Kimura, D. 1982. Left-hemisphere control of oral and brachial movements and their relation to communication. *Philosophical Transactions of the Royal Society*, **298**, 111–134.

Kimura, D., & Archibald, Y. 1974. Motor function of the left hemisphere. *Brain*, **97**, 337–350.

Kishimoto, H., Kuwahara, H., Ohro, S., Takazu, O., Nakano, H., et al. 1987. Diseases in association areas found in chronic schizophrenia using ^{11}C-glucose PET (Positron emission tomography). In R. Takahashi, P. Flor-Henry, J. Gruzelier et al. (Eds.), *Cerebral dynamics, laterality, and psychopathology*. Amsterdam: Elsevier. Pp. 555–560.

Klawans, H. L., Bergen, D., Bruyn, G. W., et al. 1974. Neuroleptic-induced tardive dyskinesia in nonpsychotic patients. *Archives of Neurology*, **30**, 338–339.

Kolakowska, T., Williams, A. O., Ardern, M., & Revely, M. A. 1986. Tardive dyskinesia under 60 years of age. *Biological Psychiatry*, **21**, 61–169.

Kolb, B., & Milner, B. 1981. Performance of complex arm and facial movements after focal brain lesion. *Neuropsychologia*, **19**, 491–503.

Kraepelin, E. 1919. *Dementia praecox and paraphrenia*. Edinburgh: E.&S. Livingston.

Lewis, D. A., Morrison, J. H., & Goldstein, M. 1988. Brainstem dopaminergic neurons project to monkey parietal cortex. *Neuroscience Letters*, **86**, 11–16.

Lhermitte, F. 1986. Human autonomy and the frontal lobes. II. Patient behavior in complex and social situations. The "environmental dependency syndrome." *Annals of Neurology*, **19**, 335–343.

Lhermitte, F., Pillon, B., & Serdaru, M. 1986. Human autonomy and the frontal lobes. I. Imitation and utilization behavior: A neuropsychological study of 75 patients. *Annals of Neurology*, **19**, 326–334.

Mathew, R. J., Duncan, G. C., Weinman, M. L., & Bar, D. L. 1982. Regional cerebral blood flow in schizophrenia. *Archives of General Psychiatry*, **39**, 1121–1124.

Mathew, R. J., Meyer, J. S., Frances, D. J., Schoolar, J. C., Weinman, M., & Mortel, K. F. 1981. Regional cerebral blood flow in schizophrenia: A preliminary report. *American Journal of Psychiatry*, **138**, 112–113.

McGlashan, T. H., & Carpenter, W. T. 1976. Postpsychotic depression in schizophrenia. *Archives of General Psychiatry*, **33**, 231.

Mesulam, M. -M. 1986. Frontal cortex and behavior. *Annals of Neurology*, **19**, 320–324.

Miller, N. E., & Cohen, G. D. Eds. 1987. *Schizophrenia and ageing: Schizophrenia, paranoia, and schizophreniform disorders in later life*. New York: Guilford Press.

Miller, R., Wickens, J. R., & Beninger R. J. 1984. Dopamine D-1 and D-2 receptors in relation to reward and performance: A case for the D-1 receptor as a primary site of therapeutic action of neuroleptic drugs. *Progress in Neurobiology*, **34**, 143–183.

Mukherjee, S. 1984. Tardive dysmentia: A reappraisal. *Schizophrenia Bulletin*, **10**, 151–153.

Murphy, D. L., Brodie, H. K. H., Goodwin, F., & Bunney, W. E., Jr. 1971. Regular induction of hypomania by L-DOPA in bipolar manic-depressive patients. *Nature*, **299**, 135–137.

Myslobodsky, M. S. 1986. Anosognosia in tardive dyskinesia: 'Tardive Dysmentia' or 'Tardive Dementia'? *Schizophrenia Bulletin*, **12**, 1–6.

Myslobodsky, M., Holden, T., & Sandler, R. 1985a. Parkinsonian symptoms in tardive dyskinesia: A prevalence study. *South African Medical Journal*, **66**, 69–72.

Myslobodsky, M. S., Tomer, R., Holden, T., Kempler, S., & Sigal, M. 1985b. Cognitive impairment in patients with tardive dyskinesia. *Journal of Nervous and Mental Disease*, **173**, 156–160.

Nelson, H. E., Pantelis, C., Carruthers, K., Speller, J., Baxendale, S., & Barnes, T. R. E. 1990. Cognitive functioning and symptomatology in chronic schizophrenia. *Psychological Medicine*, **20**, 357–365.

Owens, D. G. C. 1985. Involuntary disorders of movement in chronic schizophrenia. The role of illness and its treatment. *Psychopharmacology. (Suppl.)***2**, 79–86.

Panksepp, J. 1982. The pleasure in brain substrates of foraging. *The Behavioral and Brain Sciences*, **5**, 71–72.

Rechtschaffen, A. 1978. The single-mindedness and isolation of dreams. *Sleep*, **1**, 97–109.

Richardson, M. A., Pass, R., Bregman, Z., & Craig, T. J. 1986. The prevalence of tardive dyskinesia and depressive symptoms in schizophrenia. *Psychopharmacology Bulletin*, **21**, 130–135.

Saldate, M. C., & Orrego, F. 1977. Electrically induced release of [^{3}H]dopamine from slices obtained from different rat brain cortex regions. Evidence for a widespread dopaminergic innervation of the neocortex. *Brain Research*, **130**, 483–494.

Sechenov, I. 1893. Cited by Ratliff, F. 1962. Some interrelations among physics, physiology, and psychology in the study of vision. In S. Koch (Ed.), *Psychology: A study of science*. New York: McGraw-Hill. Vol. 4, pp. 417–482.

Sheppard, G., Manchanda, R., Gruzelier, J., et al. 1983. Positron emission tomographic scanning in predominantly never-treated acute schizophrenic patients. *Lancet*, **2**, 1448.

Singh, M. M., & Kay, S. R. 1979. Dysphoric response to neuroleptic treatment in schizophrenia: Its relationship to autonomic arousal and prognosis. *Biological Psychiatry*, **14**, 277–294.

Szechtman, H., Nahmias, C., Garnett, E. S., Firnau, G., Brown, G. M., Kaplan, R. D., & Cleghorn, J. M. 1988. Effects of neuroleptics on altered cerebral glucose metabolism in schizophrenia. *Archives of General Psychiatry*, **45**, 523–532.

Tarsy, D. 1983. Neuroleptic-induced extrapyramidal reaction: Classification, description and diagnosis. *Clinical Neuropharmacology*, **6**(Suppl. 1), 9–26.

Tonkonogi, I. M. 1973. *Vvedenie v klinicheskuju neuropsychologiuju [Introduction to clinical neuropsychology.]* Leningrad: Medgiz. [in Russian]

Tork, I., & Turner, S. 1981. Histochemical evidence for a catecholaminergic (presumably dopaminergic) projections from the ventral mesencephalic tegmentum to visual cortex in the cat. *Neuroscience Letters*, **24**, 215–219.

Uchino, J., Nakane, Y., Ohta, Y., Hirota, N., Yonekura, M., & Mori, H. 1987. Correlations between regional cerebral blood flow and clinical symptoms in schizophrenics. In R. Takahashi, P. Flor-Henry, J. Gruzelier, et al. (Eds.), *Cerebral dynamics, laterality, and psychopathology*. Amsterdam: Elsevier. Pp. 513–518.

Valenstein, E. S. 1971. Channeling of responses elicited by hypothalamic stimulation. *Journal of Psychiatric Research*, **8**, 335–344.

Waddington, J. L. 1987. Tardive dyskinesia in schizophrenia and other disorders: Association with ageing, cognitive dysfunction and structural brain pathology in relation to neuroleptic exposure. *Human psychopharmacology*, **2**, 11–22.

Widen, L., Bergstrom, M., Blomquist, G., et al. 1983. Positron emission tomography studies of brain energy metabolism in schizophrenia. In W. D. Heiss, & M. E. Phelps (Eds.), *Positron emission tomography studies of the brain*. Berlin: Springer-Verlag. Pp. 192–195.

Wilson, I. C., Garbutt, J. C., Lanier, C. F., Moylan, J., Nelson, W., & Prange, J., Jr. 1983. Is there a tardive dysmentia? *Schizophrenia Bulletin*, **9**, 187–192.

Wise, R. A. 1982. Neuroleptic and operant behavior: The anhedonia hypothesis. *The Behavioral and Brain Sciences*, **5**, 39–87.

Wolf, M. E., Ryan, J. J., & Mosnaim, A. D. 1983. Cognitive functions in tardive dyskinesia. *Psychological Medicine*, **13**, 671–674.

Wolkin, A., Jaeger, J., Brodie, J. D., et al. 1985. Persistence of cerebral metabolic abnormalities in chronic schizophrenia as determined by positron emission tomography. *American Journal of Psychiatry*, **142**, 564–571.

Zac, R. F., & Weinberger, D. R. 1986. Brain areas implicated in schizophrenia: A review and synthesis. In H. A. Nasrallah & D. R. Weinberger (Eds.), *The neurology of schizophrenia*. Amsterdam: Elsevier. Pp. 175–206.

Zimmerman, S., & Hermesh, H. 1991. *Medication-related changes of imitative praxis in schizophrenia*. Unpublished manuscript.

Zuckerman, M., & Lubin, B. 1965. *Manual for the multiple affect check list*. San Diego: Educational and Industrial Testing Service.