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Cognitive and motor retardation during writing and drawing tasks in depressed inpatients

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CONTENTS

Chapter 1

INTRODUCTION

"The patient is sitting motionless, slightly bending forward, hanging her head, knees apart, staring downwards into eternity.

When I call her name softly in the waiting-room, she does not turn her head; slowly, a little shakily, she eases herself to her feet then creeps past me in the direction in which I am pointing. Scarcely a glance, I cannot catch her eye. In my consulting room, she sinks slowly onto the chair opposite me and assumes the same as before.

She does not move when my eyes turn in her direction, looking at a deeply-lined face, the furrows in her forehead, the drooping eyelids and sagging corners of her mouth. There is a little sigh, a slight moan. Shoulders hunched, slightly bending forward, hands palm-upwards lying heavily in her lap, knees apart, feet pointing outwards flat on the floor. My question of what can I do for you is met with silence, which emphasizes the worlds between us, then sluggishly she utters the words that I have heard in our previous encounters: I'm exhausted, the last syllables hardly audible as they are swallowed by the rift between us."

The daily clinical experience of a psychiatrist, dealing with the slowing of the depressed patient in all its diversity, forms the starting point and the fundament of this thesis. Since the Hippocratic writers in the fourth and fifth centuries B.C., psychomotor changes have become widely recognised as a major symptom of affective disorders, e.g. melancholia. In his overview of "Melancholia and depression: from Hippocratic times to modern times" (1986), Jackson describes how central these psychomotor signs were in the different conceptions of melancholia in the 17th, 18th and 19th centuries. Following Parker (Parker et al., 1992) it can be stated that after the influential paper on melancholia by Freud (Freud, 1916) more accent has been put on the cognitive and intrapsychic symptoms than on the behavioural signs of depression. However, since the discovery of antidepressive medication, interest in psychomotor retardation has been steadily growing. From the beginning of the use of these drugs, it has been the clinical impression of many psychiatrists that prescribe them, that the patient has more chance of responding successfully to the drug, if he presents with some signs of psychomotor slowing (Bielski and Friedel, 1976). In the past twenty years it has been demonstrated, first by Widlöcher

et al. in the development of the Salpêtrière Retarda-tion Rating Scale (Widlöcher, 1983a and b; Widlöcher and Ghozlan, 1989) and later by Parker et al. in the development of the Core-system (Parker and Hadzi-Pavlovic, 1996), that the symptom of psychomotor retardation alone could explain a large part of the variance in the depressive syndrome, i.e., of the melancholic and psychotic subtypes. According to the former authors, psychomotor retardation can be considered as the core behavioural pattern or the primary disorder in depression. However, this opinion is not commonly accepted. Other authors consider the psychomotor symptoms to be on the same level as other symptoms of the depressive syndrome, e.g. the DSM IV classification (American Psychiatric Association, 1994) or group them into a separate and independent syndrome, comparable with fever in internal medicine (Bermanzohn and Siris, 1992).

Furthermore many differences subsist in the definitions of psychomotor retardation and agitation and various methods can be used to measure and analyse them. One can broadly discern between two ways of defining these phenomena. The use of fairly "narrow" definitions means that only the motor behaviour manifested in facial expression, speech, gross and fine motor activity is taken into account. "Wider" definitions not only encompass motor behaviour, but also mental activities, e.g. disturbances of attention, memory and the experience of time, hedonia and vital functions, such as sleep, eating behaviour and sexual libido. In the latter definitions, the underlying assumption stresses that retardation determines both motor and mental behaviour.

An overview of the literature from the past fifteen years about different methods used to measure psychomotor retardation in depressed patients is provided in Chapter 2 of this thesis. The results obtained with the following methods are summarised and discussed: (1) observation and rating scales, (2) observation, coding and analysis of non-verbal behaviour, (3) speech analysis, (4) (choice) reaction time tasks, (5) measurement and analysis of gross and (6) fine motor behaviour.

The aim of the research reported in this thesis is to contribute to a better understanding of the changes in psychomotor behaviour in depressed patients, by learning about the symptom itself. In a group of patients suffering from a Major Depressive Episode, accor-

ding to the DSM III-R criteria, fine motor behaviour was measured in great detail, using standard methodology, with the primary aim of obtaining a much more extensive and refined description than the 'de visu' clinical description of the slowing phenomena. Secondly, the cognitive and motor aspects of psychomotor slowing that were uncovered in this way were studied and invoked interest in studying the cognitive and/or motor processes that change in depressed patients. Therefore a methodology was used, introduced by Van Hoof et al. (1989) that consists of measuring and analysing fine motor behaviour in writing and drawing tasks. With the help of a graphics tablet (digitiser), a specially designed pen to measure pen pressure and a personal computer, the writing and drawing movements of the depressed patient were recorded and analysed in great detail. This new technology was used to study the psychomotor disturbances of depressed patients in an explorative and descriptive way. Therefore a broad variety of tasks were designed that differed in nature and complexity (see Appendix). In the first part of the test, the subject was asked - on analogy with the standard counting task - to write the numbers 1 to 10 and also to write a simple text of four lines, containing twenty words. He was also asked to read the numbers and the text aloud. This part of the test is not presented in this thesis. In the second part, the subject was asked to do very simple drawing movements with the pen, i.e., rapid up and down movements, to draw lines between targets and to draw lines freely. It was assumed that these tasks mainly rely on motor processing and do not require higher order cognitive processes. Finally, in the third part, the subject was asked to copy simple and complex figures, in which the cognitive and motor demands were manipulated.

In the first studies that were conducted with this new method by Van Hoof et al (1993) and Van Mier and Hulstijn (1993), only these figure copying tasks were used. The results of the depressed patients in these studies, compared to those of normal control persons, are presented in Chapter 3.

In line with these studies, we firstly analysed the figure copying tasks in part three of the test, i.e., the copying of lines and simple figures (angle and circle; diamond and spiral), copying complex figures or rotating the figures. The depressed patients were compared

to normal healthy controls in order to investigate whether the depressed patients were slower in accomplishing these tasks than the control persons, and if so, in which aspects of psychomotor behaviour this slowing was most apparent. The results of this study are presented in Chapter 4.

We also compared the amount and nature of the slowing that was found in depressed inpatients after the start and at the end of a standard treatment in which antidepressive medication (fluoxetine) was administered. This study is described in Chapter 5.

In the studies described in Chapters 4 and 5, we found indications of slowing of the motor processes themselves in the depressed patients. Therefore we performed a detailed analysis of the results of the simple drawing movements in the second part of the test. This was the objective of the study that is presented in Chapter 6.

The next step of the study was to compare this "more pure" motor slowing in depressed patients who were receiving the same treatment as that described in Chapter 5, to the performance of a control group. Once again, measurements were performed after the start and at the end of treatment. The results are presented in Chapter 7.

The thesis is concluded by a general discussion (Chapter 8) and a summary.

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THE MEASUREMENT OF PSYCHOMOTOR RETARDATION IN DEPRESSION

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Abstract

This review contains an overview of the literature of the past fifteen years on psychomotor retardation in depressed patients, as measured by the following methods: (1) rating scales, (2) observation, coding and analysis of specific non-verbal behaviour, (3) speech research, (4) (choice) reaction time tasks, (5) analysis of gross motor activity and (6) of fine motor behaviour. In each section the results of the different studies are summarized in order to examine whether a retardation was established in the depressed patients, how the retardation manifested itself and what its nature was (cognitive and/or motoric). Correlations with data obtained with other methods and treatment effects also are reported.

Keywords: psychomotor slowing, retardation, depression, rating scales, non-verbal behaviour, speech, reaction time tasks, actometry, fine motor behaviour.

Through the years psychiatry in the low countries has paid much attention to the role and function of psychomotor activity in normal psychological functioning, and to psychomotor changes and psychomotor retardation in psychopathology Attention focused on psychomotor behaviour as a mode of expression (Carp, 1947), that is as a means to articulate and give form to conscious and subconscious drives (Rumke, 1954) Thus, in the psychomotor disorders of depression and melancholia, disturbances in temperament, drives and character became manifest (Carp, 1947) In a phenomenological sense, these psychomotor alterations were viewed as a sign of a disharmonious relationship with the social environment (in der Welt sein)

Present-day psychiatry also regards psychomotor alterations as important symptoms of, in particular, the depressive syndrome As a result of changes in methods of diagnosis and classification, however, they are now viewed as more or less separate from the personality, notably as a mental symptom in its own right How psychomotor changes are to be defined, however, remains unclear The multitude of denominations alone constitutes a source of confusion psychomotor disturbances or even disorders or alterations, psychomotor retardation, slowing, inhibition, sometimes used as a generic term, at other times to distinguish it from psychomotor agitation, hypokinetic and akinetic syndrome, bradyphrenia or bradypsychia, motor poverty syndrome, psychotic motor syndrome, etcetera These diverse terms can be divided into two groups The more narrow definitions merely concern motor behaviour, such as facial expression, speech, gross and fine motor skills The broader, however, do not only encompass motor behaviour, but also mental activities, such as attention, memory, time perception, hedonism, and even vital functions such as sleep, eating and sexual libido

In addition to the unclarity about the definition of psychomotor disorders, three different viewpoints exist about their relationship with other depressive symptoms According to the first, some authors consider psychomotor disorders as a symptom of the same order

as other symptoms (DSM-IV; American Psychiatric Association, 1994), or as a key symptom of all mood disorders, some related syndromes or subgroups. Thus psychomotor changes have been associated with endogenous depression (Günther et al., 1988), with the bipolar disorder (Lykouras et al., 1986), with the vital and the melancholic subtype (Rush and Weissenburger, 1994; Parker et al., 1993a; Parker et al., 1994; Parker and Hadzi-Pavlovic, 1996) and/or the psychotic subtype (Parker et al., 1994), or with certain depressive symptoms, e.g. eating disorders (Browning and Cowen, 1986).

A second view classifies a number of psychomotor symptoms as a separate syndrome with its own etiology, pathogenesis and psychoneurophysiology, in line with for instance fever as an independent syndrome of various internal diseases. The 'akinetic' syndrome (Bermanzohn and Siris, 1992) and the 'psychotic motor syndrome' (Günther et al., 1988) are examples of this latter viewpoint.

A third view conceptualizes psychomotor alterations as the primary disorder of the depressive syndrome (Widlöcher, 1983 a and b). To substantiate this view Widlöcher argues that, in factor analyses, the disorder can explain or cluster a substantial proportion of the variance of the depressive symptomatology (up to 65%), generates new insights into the etiology and pathogenesis of depression and finally, that it has predictive value regarding therapeutic effects of antidepressants and electroconvulsive therapy (see Joyce and Paykel, 1989).

Finally, various measuring techniques are applied which, in all probability, measure different aspects of psychomotor retardation, making a comparison of the results difficult. For instance, can the prolongation of Speech Pause Times during counting from 1 to 10 be compared with the increase in pause times when writing down the numbers of 1 to 10? In these instances the theoretical frames of reference can differ strongly in the various studies and a common framework may be lacking. Numerous approaches and models are possible, such as: cognitive psychological, information processing, stress-physiological, chronobiological, interactional, pharmacological, structural, neurophysiological, etcetera. In this article we provide an overview of the methods used to measure psychomotor retardation, as they are defined in the respective studies, and of the results

that were obtained. Only those studies whose data were both statistically analysed and relevant for the subject 'psychomotor retardation' are discussed. In the discussion of the results the following questions are posed in each case: (1) Did the applied measuring technique establish a retardation in the depressed patients (as compared to their non-depressed state, normal controls or other psychiatric or neurological control groups)? Was this retardation more specific for a certain subgroup of depressives? (2) If so, how did the retardation manifest itself? (3) If so, was the nature of the retardation more closely defined, for instance as cognitive and/or motoric? (4) Were there any correlations between the results found with the measuring technique applied and the data obtained by other methods? (5) Were effects of treatment on the retardation indicated and if so, what effects were found? And finally, whenever the authors placed their findings in a specific theoretical frame of reference, this will be noted.

The measuring techniques that will be described are put into six categories: (I) rating scales, (II) the measurement and analysis of specific non-verbal behaviour, (III) speech research, (IV) reaction time measurements, (V) measurements of gross motor behaviour, and (VI) the study of fine motor behaviour.

I. Rating scales

The most widely known rating scale of psychomotor retardation, the Salpêtrière Retardation Rating Scale (SRRS), was developed in Paris by Widlöcher et al. (1983a and b; Widlöcher and Ghozlan, 1989). The SRRS consists of 15 items (14 items plus a final appreciation), classified into four subscales: three motor items (gait, trunk and limb movements, facial expression), three speech items (speech rate, voice modulation and intensity, brevity of answers), two items concerning objective mental activity (fluency of thought and richness of association), and six items reflecting subjective mental activity (ruminating or worrying, fatiguability, interest, perception of time, memory, and concentration). The scale has been validated with large groups of both in- and outpatients.

Factor analytic studies showed that all items had a high load on the first factor, which explained approximately 60% of the variance (Widlöcher, 1983a and b); two other factors accounted for about 7 to 9% of the variance. The first factor opposes the motor and mental items, the second factor contrasts the objective and subjective mental items. The principal component analysis, however, showed one unique and general process and a relationship between motor retardation and mental slowness that was stronger than generally assumed (Widlöcher and Ghozlan, 1989). In repeated studies of groups of depressed patients it was also found that the factor analytic structure remained very stable (Jouvent et al., 1980 and 1981; Pellet et al., 1982; Granier et al., 1983; Widlöcher, 1983a and b). Using the SRRS, retardation was found to correlate highly with the severity of the depression as indicated by the Hamilton Depression Rating Scale (HDRS) (Hamilton, 1960) and the Montgomery Asberg Depression Rating Scale (MADRS) (Montgomery and Asberg, 1979). Significant correlations were also observed between the retardation scores before treatment and the degree of improvement as reflected in the difference on the HDRS between day 0 and day 25 (Widlöcher, 1983a).

The SRRS was used in many studies (Jouvent et al., 1980 and 1981; Granier et al., 1983; Pellet et al., 1982; Lecrubier et al., 1986; Widlöcher, 1986). Its scores showed a varying relationship with the results of other measuring techniques. Between the SRRS scores of bi- and unipolar depressed patients and the Speech Pause Time (SPT) positive correlations were observed (Hoffmann et al., 1985) (see section III. Speech). Hardy et al. (1984) found a strong correlation between the decrease of the SRRS scores after treatment and the shortening of the SPT. The SRRS scale was also applied in actometric research resulting in varying correlations between the retardation scores and actometric variables (Royant-Parola et al., 1986; Raoux et al., 1994). Smith et al. (1994), however, observed a negative correlation between psychomotor retardation measured with a subscale of the SRRS, and commission errors ('false alarms') in a signal-detection task. These results led them to conclude that the cognitive disorders in depressed patients consist of two dimensions: a general cognitive deficit and a specific effect of retardation. The SRRS was translated into Dutch by Van de Berg and Van Bavel (1990; not published). Very recently a new translation was published, the 'Widlöcher Remmingsschaal'

(WRS) The scale was validated in three separate studies in which in- and outpatients with a depressive disorder or schizophrenia participated Reliability (N=26), concurrent and divergent validity (N=25), and predictive validity (N=28) were examined respectively (de Weme et al , 1996) The internal consistency was good and the interrater reliability was sufficient to good Convergent and divergent validity were demonstrated by comparing the correlation between the sum scores on the WRS and those on the retardation items of the Comprehensive Psychopathological Rating Scale (CPRS) (r=0 91) with the correlation between the sum scores on the WRS and the MADRS (r=0 40) The decrease of the sum scores on the WRS after two weeks of treatment with antidepressants predicted remission after six weeks

Like other rating scales SRRS has its limitations, e g the subjective component of the researcher's assessment and in research the necessity of large, heterogeneous groups of patients

Parker et al (1990, 1993a) have drawn up an 18-item questionnaire that allows an overall scoring, called CORE score, of psychomotor changes in depression Factor analytic and LCA (Latent Class Analyses) research has led to a 'tree analogy' to classify these disorders nine items concern 'non-interactiveness' (the trunk), three refer to 'retardation' (branch 1) and six to 'agitation' (branch 2) The factor retardation explained 77% of the variance, the factor agitation 18% and the factor non-interactiveness 6% This last factor intercorrelated highly with the factor retardation (r=0 65) and with the factor agitation (r=0 45), and appeared to underlie both factors Higher scores on these various factors have been associated with clinical features of endogenous depression or melancholia (Parker et al , 1990 and 1994) Parker et al argue that psychomotor disturbance is specific to the melancholic subtype of the depressive syndromes, in this context they repeatedly refer to the work of the DSM-IV Task Force, who, in nine operational definitions of the melancholic (endogenous) concept, found that psychomotor retardation was the only symptom that recurred in all definitions (Rush and Weissenburger, 1994) In the research by Parker et al (1993a, 1994) this subgroup of patients was characterized by a relatively high age, an initial depressive episode later in life, a larger number of more severe depressions, a higher incidence of delusions and hallucinations, a greater chance of total

remission, and a positive response to tricyclic antidepressants (Parker et al , 1993b) and electroconvulsive therapy (Hickie et al , 1990 and 1996) Higher factor scores correlated moderately with the clinical assessment of the severity of the depression and with the Hamilton scores, but proved independent of the Zung scores The total Core scores correlated strongly with reaction times in a simple reaction time task, a number recognition task and a trail-making test (Parker et al , 1994) A relationship with dexamethasone non-suppression was also established (Mitchell et al , in press, Parker and Hadzi-Pavlovic, 1996) Moreover, melancholic and non-melancholic patients could be differentiated on the basis of ten psychosocial risk factors (Parker et al , 1991)

Very recently research results have been published that confirm the predictive and comparative validity of both measuring techniques, the SRRS and the CORE system (Hickie et al , 1996) Both scales proved to be able to predict the response on electroconvulsive therapy, for 6 treatments as well as for a complete series of treatments The retardation and agitation subscales of the CORE system, though not correlated themselves, showed strong correlations with the total CORE score and with the subscale non-interaction All subscales of the SRRS showed strong intercorrelations This confirms Widlocher's proposition that the SRRS mainly measures a single dimension, viz psychomotor retardation The CORE system, however, clearly also measures a dimension of agitation The scores of the SRRS and those of its subscales proved to be strongly correlated with the total CORE score (r=0 83) and with the scores of the subscales retardation (r=0 83) and non-interaction (r=0 77), though not with the subscale agitation (r=0 25)

II. The measurement and analysis of specific non-verbal behaviour

Measuring and analysing specific non-verbal behaviour entails the monitoring, classifying and analysis of specific behaviours and movement patterns, such as eye contact, gazing, hand movements and posture This type of research is conducted under naturalistic

conditions, i.e., according to ethological principles. For an overview, from which the following data have been taken, we refer to Le Cloître et al. (1993) (pp 211-212; 216-218).

In behavioural studies like these, agitation and retardation were usually examined strictly independently. In a video analysis Ulrich and Harms (1985) (in Le Cloître et al., 1993, pp 211-212) for instance described two different types of agitation and one form of retardation. The latter was expressed in fewer eye movements, diminished facial expressions, a constricted posture, a deepened voice and impoverished speech. They also noted that retardation and agitation can sometimes coincide; in such cases agitation was reflected in an unrest in gross motor behaviour and a large number of hand movements (also see Jones and Pansa, 1979). This combination of agitation and retardation can be very disturbing and stressful for the patient.

By means of sophisticated algorithms Frey et al. (1980) (in Le Cloître et al., 1993, pp 212 and 216-217) determined an individual movement 'gestalt'; applying the same methodology to 13 depressed inpatients Fisch et al. (1983) found a reduction in mobility (the duration of being in motion), in complexity (the degree of simultaneous movement of various parts of the body), and in dynamic activation (the speed at which movements are initiated or completed). The effects of treatment were also studied. After successful therapy patients exhibited on the one hand a drop in pause times (see below), and in self-touching (Jones and Pansa, 1979), and on the other hand an increase in general activity (see below), smiling and staring (Jones and Pansa, 1979), and an increase in the number, diversity and complexity of movements (Fisch et al., 1983; Schelde et al., 1988).

Various studies (again see Le Cloître et al., 1993, pp 217-218) further showed an increase in, particularly, social and communicative behaviour after treatment. In addition, an improvement in the total picture of body coherence and coordinated motor behaviour was observed. Fisch et al. (1983) found that the individual movement characteristics, the idiosyncratic features or 'signature' of the movement pattern of the individual, resurfaced as the patient recovered from the depression.

Bouhuys and Alberts (1984) used a method to describe and quantify the timing of various behaviours of the participants in a conversation, such as looking, hand movements, and

head movements, in relation to speech and pauses They presented evidence that in a group of depressed patients (N=31) "relational" behaviours (i e , looking, nodding, gesturing) occurred less in patients who would improve, whereas "non-relational" behaviours (i e , intensive body touching, head movements) occurred more in these patients than in those who did not improve (Bouhuys et al , 1987) The predictive power of these variables could not be explained by their relationship with the baseline severity of depression, which in itself also predicted improvement

In later studies they focused on the interactional processes between severely depressed patients and the psychiatrist by direct observation of their behaviour during an interview Using ethological methods, they indirectly investigated retardation phenomena in depressed patients In their analyses of the patients' behaviour (N=61) they identified five factors, i e , restlessness (leg and hand movements), speech, active listening (head movements and intensive body touching during listening), eagerness (yes-nodding and no-shaking) and speaking-effort (looking, gesticulating, head movements during speaking) (Bouhuys et al, 1991) It appeared that patients who did not improve (N=13) displayed more speaking-effort and less active listening than those who did improve (Bouhuys and Albersnagel, 1992) The analysis of the psychiatrist's behaviour revealed seven factors (Bouhuys and Van den Hoofdakker, 1991) restlessness 1 (head and leg movements, object touching) and restlessness 2 (body touching, head movements), speech (speech, gesticulating, movements and gesticulating during listening), active listening (intensive body touching and hand movements), turn-taking (leg movements and gesticulating during listening), encouragement (back-channel behaviour and nodding), and change-looking (looking and head movements) It was found that restlessness 2, speech, encouragement and active listening could be 'predicted' from observed behaviour of the patients The psychiatrist displayed low levels of active listening and showed a greater tendency towards encouragement in his interaction with patients who did not improve (Bouhuys and Van den Hoofdakker, 1993) At the same time the psychiatrist exhibited an aversive response to the non-improved patients he more frequently looked away during his encouragement It appeared that also in patients with seasonal affective disorder (SAD) a number of these behavioral variables of the patients and the intervie-

wers predicted the response to light treatment (Geerts et al , 1995) In a later study it was found that the more attunement (i e , the absolute difference between patients' and interviewers' nonverbal behaviour) increased over the interview, the more favourable the subsequent course of the depression was (Geerts et al , 1996) In a recent study Bouhuys et al (1996) showed that deficits in the decoding of facial emotional expressions may play a role in the persistence of depression They followed the course of depression during 30 weeks in 33 outpatients The course was less favorable in patients who perceived less sadness, rejection or anger in schematic faces (line drawings)

Finally, Katsikis and Pilowsky (1991) and Pilowsky and Katsikis (1994) used a computerized taxonomic methodology by which they quantified facial expressions, more in particular smiling Comparisons between depressives, patients suffering from Parkinson's disease and normal controls showed significant group differences

III. Speech

In the 50s, 60s and 70s several studies already reported alterations in, e g speech rate and speech volume in manic, depressive as well as phobic patients (see review article by Greden and Carroll, 1981) The work of Szabadi et al (1976) is seen as a milestone because it allowed a reliable measurement of the various speech segments using oscilloscopic tracings and voice prints During an automatic speech task (counting from 1 to 10) Szabadi et al (1976) compared four unipolar depressives with normal controls and observed in the patients a prolongation of Speech Pause Time (SPT) whereas Phonation Time (PT) remained unchanged The increase in SPT disappeared after treatment with 100-150 mg of amitriptyline hydrochloride This study was replicated twice by Greden and Carroll (1980) and by Greden et al (1988), and extended to bipolar patients, their findings corresponded highly with the Szabadi study and confirmed the hypothesis that SPT-elongation was a state-dependent feature of psychomotor retardation in depression

Hoffmann et al (1985) measured the SPT in 22 depressed patients (12 unipolar and 10 bipolar) not receiving any medication, in three tasks counting from 1 to 10, reading 10 numbers in a random order and reading aloud the alphabet When the unipolar patients were grouped with the retarded bipolar patients (SRRS score > 10) the SPT of this group was found to be significantly longer than that of the controls and the non-retarded bipolar patients The SPT of the first task also showed a correlation with the reaction time in a simple reaction time task (pressing a button after an auditive signal) The SPT correlated positively with the SRRS scores in the unipolar and bipolar patient groups The diurnal variations in the SPT found by Greden et al in earlier experiments were, in this study, only replicated in the controls No correlations were found between the SPT and latencies of REM sleep, nor between the SPT and post-dexamethasone levels of cortisol in the blood In ten patients who were treated with amitriptyline (150 mg/day) for four weeks it was established that the decrease in the SPT correlated positively with lower scores on the HDRS

Later research by Nilsonne (1987, 1988), resulted in a much more complex picture of speech disturbances in depressed patients It pointed out that different types of speech, such as reading aloud, spontaneous speech and counting, could be affected in different ways during a depression In a comparison of 28 depressed patients with 13 healthy control subjects significant differences were found between the two groups, particularly in three variables relating to the fundamental frequency (F_0) the mean rate of change in F_0, the standard deviation of this change and the standard deviation of the F_0 distribution In 16 patients who improved clinically, both the changes of these variables and the percentage of pause time correlated with the clinical condition as measured by the Comprehensive Psychopathological Rating Scale (Asberg et al , 1978) However, no differences were found in the time needed to read a text, the pause times during reading, the total time needed to count from 1 to 10 and the pause times in this latter task In a brief interview he did find, though, that the pause times between the researcher's questions and the subject's responses were significantly longer in the depressed patient group The author asked himself what the observed deviations in the speech variables signified were they to be viewed as indicators of retardation, did they point to an

underlying neurophysiological disorder; or were they the expression of the patient's feelings of sadness and grief? Nilsonne considered the view that psychomotor retardation could be quantified by the use of speech variables a simplification of the complex interaction between factors that influence speech rate and the incidence of pause times. He argued that the typical 'voice of depression' (in retardation: slow, hesitant, monotonous, level and weak; in case of agitation: tremulous, nervous, quivering, high-pitched and staccato) (Greden, 1993) was the result of many factors interacting, e.g. the type of depression, the degree of psychomotor retardation, age, sex and personality. Selecting a limited number of speech variables relevant to the study of depression posed the key problem to Nilsonne.

In the mean F_0 and the F_0 range of 14 depressed patients Bouhuys et al. (1990) detected a clear circadian pattern, reaching its peak at about 4 pm. They described the fluctuations in these parameters and the changes in mood during and after total sleep deprivation. These alterations showed hardly any correlation and the authors suggested they might be regulated by different mechanisms.

Flint et al. (1993) compared 30 depressives, 30 patients suffering from Parkinson's syndrome and 31 healthy controls with respect to three acoustic parameters of articulation. The patient groups displayed a shorter voice onset time (VOT) and a lowered second formant transition; the depressed patients exhibited an increased spirantization (i.e., voice related noise during what would normally be complete closure of the vocal tract; it reflects 'leakage' of the vocal tract, e.g. during the closure interval of stop consonants). However, no differences were observed between the two patient groups. The authors suggested a nigrostriatal dysfunction as the cause of these articulation disorders.

During two weeks of treatment Kuny and Stassen (1993) took six measurements on 30 depressed patients. The experimental set-up and the design were analogous to earlier research in which no relationship had been found between changes in individual speech parameters and psychopathological improvement (Stassen et al., 1991). In the 1993 study they recorded 16 variables with regard to speaking behaviour and voice sound characteristics during (*1*) counting aloud from 1 to 30, (*2*) reading an emotionally neutral text aloud, and again, (*3*) a renewed counting aloud from 1 to 30. Compared to a large group of

normal, healthy control persons (N=192), the patient group differed in (*1*) total speaking time, (*2*) the total duration of pauses/words, (*3*) energy/dynamics, (*4*) fundamental frequency (F_0), (*5*) F_0 amplitude, and (*6*) F_0-6db range Variables 1 and 2 normalized after treatment, variables 3 to 6 still showed a significant difference between the two groups after treatment Distinct correlations were found between the clinical parameters (the scores on the HDRS items and the AMDP syndromes) (Arbeitsgemeinschaft für Methodik und Dokumentation in der Psychiatrie) (de Cuypere et al , 1990) and the changes in F_0 amplitude, F_0-6db range and F_0 contour, as well as between the parameters energy and dynamics A further important difference that was observed between the data before and after treatment was before treatment the patient group displayed a far smaller degree of between-subject variation than the control group, this variation increased notably after treatment, without, however, reaching the degree found in the normal population Depression appeared to even out speaking behaviour and voice sound characteristics, i e , induce uniformity in patients With improvement patients regain their individual speech characteristics

Considering all the results from the various speech studies mentioned above, it can be concluded that a genuine 'breakthrough' has not been achieved None of the approaches appears to be powerful enough to define disorders in depressed patients clearly and record changes during treatment accurately

Finally, one other type of research needs to be mentioned, viz the study that investigates the meaning of that which is uttered As early as 1967 Aronson and Weintraub showed that the verbal production of patients recovering from depression differed markedly from those of patients showing no improvement A relationship between speech parameters and the content of the spoken words was also demonstrated response latency increased with words of a depressive nature (Gotlib and Mc Cann, 1984) In ten depressed patients Vanger et al (1992) observed an increase in speech activity (the number of syllables) and the duration of silent intervals when, during a 15-minute interview, the content shifted from a neutral subject to the patient's current worries and problems Both measures were also affected by the severity of the depression

IV. Simple and choice reaction time measurements

Numerous early studies using reaction time measurements showed that depressed patients are slower than normal controls and/or non-depressive psychiatric patients (Hall & Stride, 1954; Friedman, 1964; Martin & Rees, 1966; Bruder et al., 1980) (see Cornell and Suarez, 1984). Later, tasks were employed allowing decision time (DT) and movement time (MT) to be measured separately. The subject was told to hold down a ready-button until he/she had selected the correct answer, after which he/she was to move the digit to the corresponding reply button. In this context Byrne's research (1976) on psychotic and neurotic depressives and normal controls is widely known. Both patient groups were slower than the normal controls: the delay was caused by a prolonged DT and MT. The psychotic patients proved to be slower than the neurotic depressives, which could be attributed to an even longer DT. There were, however, two major shortcomings in the design of the study: neither was there a correction for age, nor for the severity of the depression.

Cornell and Suarez (1984) used a simple reaction time task (SRT), a motor reaction time task (MRT), consisting of holding down a button and moving towards the reply button, and a cognitive reaction time task (CRT), involving the selection of the correct answer and the pressing of the relevant button by either the left or the right hand. Three subject groups were tested: melancholic patients (N=14), non-melancholic depressives (N=14) and a normal control group (N=14). The SRT did not reveal any differences between the groups, but on the MRT patients performed worse than the controls. Cornell and Suarez therefore concluded that there was an evident motor component in the retardation. The deterioration in the performance of specifically the melancholic group stood out when the degree of complexity of the cognitive task was increased.

Jansen and Siegfried (1984) compared elderly depressives who were either treated with nomifensine, or with a placebo. The DT, and not the MT, was found to vary between the two groups. Knott and Lapierre (1987) proved the absence of a relationship between DT or MT and the severity of the depression, as measured by the HDRS.

Rogers and Lees (1987) compared 30 depressed patients, 30 patients with Parkinson's syndrome and 30 normal controls using a computerized Digit Symbol Substitution Test (DST) The retardation in both patient groups consisted of a cognitive component (prolonged matching time), as well as a motor component (prolonged movement time) Differences between patient groups were not found After approximately eight months of treatment 12 depressed patients were re-tested the results showed a clear decrease in decision time, although movement time had not improved

In addition to the DST, Hart and Kwentus (1987) also availed themselves of the Sternberg short-term memory scanning test to compare 15 depressed patients with 16 normal control subjects In both tests the patients were evidently slower than the controls, the increase in response latency as a function of the size of the memory set did not differ between the two groups, which is in contrast with for instance patients with subcortical neurological dysfunctions like Friedreich's ataxia This difference seems to suggest a normal rate of information processing in depressives, Hart and Kwentus argued that the retardation might have been caused by a lack of motivation during the performance of the task

Ghozlan and Widlocher (1987) confirmed Byrne's hypothesis that only DT was sensitive to clinical improvement In a later study (1989) they compared the performances of 19 depressed patients in a choice reaction time task before and after recovery Again the results showed a decrease in DT after recovery, whereas MT was not reduced Ghozlan and Widlocher (1989) focused their study on the progression of DT and MT for the entire duration of the task, which consisted of 50 trials No differences in DT were found, but MT before treatment was shown to lenghten as the session evolved, after improvement of the depressive condition this pattern was reversed They concluded that DT and MT were based on two different mechanisms In depressed patients MT would basically not be affected, but would merely vary proportionately to the degree of agitation (also see Ghozlan and Widlocher, 1987)

In a comparison of 12 depressed outpatients with 12 healthy controls, concerning their performance on perceptual-motor tasks, recognition-memory tasks, and an analysis of eye-movements, Deijen et al (1993) found that the decision time on the choice reaction time task was longer for patients than for controls, while the motor time appeared to be

the same From various cognitive tasks it resulted that the patients performed slower on the effort demanding tasks, while no difference between groups was found in effortless tasks In addition, the range of horizontal eye movements, an indication of visual span, was found to be smaller in patients

In conclusion it can be said that retardation in depressed patients, as measured by means of simple and choice reaction time tasks, is based on a slowing of both cognitive and motor processes It has become clear that specifying both types of slowing proves to be extremely difficult Although evidence has been found that clinical improvement is accompanied by an enhancement of cognitive processes, it remains unclear whether it also generates an acceleration in motor performance

V. Gross motor behaviour

Gross motor performance is a psychomotor activity which has been the subject of study for centuries Psychological and social connotations are to be found in Schilder's well-known "Image and appearance of the human body" (1950) Major research using telemetry was conducted by Kupfer et al in the early seventies (see eight publications in the review article by Greden and Carroll, 1981) Among other findings, Kupfer et al (1974) established that bipolar patients displayed less motor activity per 24 hours than unipolar patients and that this difference disappeared as the depression cleared

In the publication by Wolff et al (1985) an overview is given of 23 studies conducted before 1985 in which (motor) activity is either examined by means of mechanical or electronic monitoring and in which the relationship is discussed between the reported findings and affective state, changes in affective state, clinical improvement, sleep criteria, diagnostic categories, biochemical parameters, the use of medication, and circadian rhythms Employing an actigraphic measurement technique Wolff et al gave a delineation of the 24-hour profiles of 27 patients in depressive, euthymic and manic state and of a group of normal euthymic controls (N=24) respectively In patients in a

depressive state they recorded a decrease in diurnal motor activity as compared to their euthymic or manic state Even in euthymic state this activity was still found to be lower than in the control group

Royant-Parola et al (1986) compared such 24-hour profiles of 12 depressives before, during and after treatment and noted that the lowest level of activity and the immobility peaks occurred before noon and at about 3 pm With clinical improvement the level of activity was found to rise gradually and the duration of immobility was reported to decrease Especially the immobility measure proved a valuable index and was found to be more sensitive than the level of activity In a further study of 10 unipolar depressives Benoît et al (1985) demonstrated a relationship between immobility parameters and the severity of the depression, in addition they described various 24-hour profiles of endogenous and non-endogenous depressives

Joffe et al (1987) reported that, of 19 depressed patients who were given carbamazepine, those who showed signs of recovery from the depression (N=7) also exhibited a significant increase in motor activity (also see Wolff et al , 1985), this increase mainly occurred from 1 to 4 pm and from 7 to 10 pm No change in motor activity was found in those patients who did not respond to the treatment (N=12) The mean baseline measurements of motor activity had no predictive value with respect to the effects of carbamazepine Motor activity in the daytime and during 24 hours generally correlated negatively with the severity of the depression, as measured by the Bunney Hamburg Scale (Bunney and Hamburg, 1963) However, positive correlations were reported between motor activity after treatment and the items motor hyperactivity and motor retardation of a modified BPRS (Brief Psychiatric Rating Scale), although the changes on the BPRS items proved not to correlate with the motor changes during treatment This is why Joffe et al (1987) concluded that it was likely that a scale such as the BPRS measured other factors than the actigraphic technique, which proved more effective to detect changes during treatment

The Salpêtriere research unit (Raoux et al , 1994) presented an actigraphic study in which earlier findings (Benoît et al , 1985, Royant-Parola et al , 1986, Dantchev et al , 1992) were replicated in a larger group of patients (N=26) As in the earlier studies the group

was tested before and after treatment with tricyclic antidepressants. Before treatment hypoactivity during the day and a generally low amplitude of the circadian rhythm was recorded. After treatment there was a substantial increase in motor activity, approaching the level of motor activity observed in normal control subjects. Incidences of phase changes were not found (no shifts in the acrophase) and the circadian pattern could be described with a simple cosine function. Raoux et al. (1994) noted that the relationship between the clinical data and motor activity, as measured by means of actometry, was not clear. Some studies showed either a correlation between nocturnal activity and self-assessments of the depression (Foster and Kupfer, 1975) or between diurnal activity and hyperactivity scores on the BPRS (Joffe et al., 1987). In other studies no correlations were found (Kupfer et al., 1974; Godfrey and Knight, 1984). In the responders Raoux et al. (1994) observed a correlation between the activity parameters before treatment and the SRRS scores, as well as a correlation between the improved mood scores on the MADRS and the rise in motor activity. They reached the tentative conclusion that a negative correlation between the baseline activity level and clinical improvement, and a trend in which responders exhibited a lower level of activity before treatment than non-responders had some predictive value with respect to motor activity.

In order to measure gross motor performance in 15 endogenous depressed patients, 15 non-endogenous depressives and 15 healthy controls Günther et al. (1988) availed themselves of the MLS (Motorische Leistungsserie) (Schoppe, 1974), the LOS (Lincoln Oseretzky Motor Development Scale) (Reinert, 1966; Günther, 1980) and of the LNB Motor Subtest (Luria Nebraska Neuropsychological Battery) (Luria, 1970; Golden, 1979). They observed a wide range of motor disturbances in the endogenous depressives, both in the treated and the untreated patients; before treatment the motor symptoms were far more explicit than after treatment. No differences were recorded between patients with unipolar and bipolar disorders, nor any systematic covariations between psychopathological and motor variables. The findings seemed to suggest a disease-related syndrome rather than a drug-related syndrome. Günther et al. (1988) referred to this syndrome as the Psychotic Motor Syndrome (PMS). It involves disturbances of lip and tongue movements, fine and gross movements of the dominant right hand, and the complex motor coordinati-

on of the limbs. The syndrome is analogous in schizophrenics and depressives; in the former it is seen as a 'trait', in the latter as 'state' marker.

Using a continuous 48-hours actometric monitoring technique, Kuhs and Reschke (1992) failed to establish a relationship between the unipolar or bipolar course of depression and psychomotor activity, nor did they find a correlation between psychomotor activity and sleep time.

It also has to be stressed that actometric registration also showed that psychomotor retardation was not only found in depressed inpatients, but that a group of eleven depressed female outpatients also exhibited a decrease in daytime activity (Futterman and Tryon, 1994).

Sachdev and Aniss (1994) measured simple and complex ballistic movements in 10 retarded melancholic patients, 10 patients with Morbus Parkinson and 10 normal controls. The simple movements consisted of angular movements of 10, 20, 30, 40 degs according to the Hallett and Khoshbin methodology (1980). The complex movements involved both sequential and simultaneous squeezing and flexion of the right hand and arm, analogous with the methodology of Benecke et al. (1986; 1987). The patient groups demonstrated a smaller increase in movement speed than the controls when the angle of rotation was extended from 10 to 40 degs. In the complex movements similar discrepancies were found between melancholic and Parkinson patients: perhaps as a result of a lowered dopaminergic function? Sachdev and Aniss (1994) underlined that the melancholic depressives had been carefully selected. The disturbances observed could not be attributed to the use of neuroleptics, nor to a lack of dedication, interest, motivation, effort or volition. In their view the depressive retardation was not to be interpreted as intrapsychic inhibition, nor as the result of the depressive mood. They supported Widlöcher's proposition that we are dealing with a 'core behavioural pattern'.

In the Hôpital de la Salpêtrière in Paris Delgado and Hereda have recently set up a new kind of research concerning the gait of depressed patients. To date no results have been published. The research expands on earlier work by Sloman et al. (1982; 1987) who, using interrupted light cinematography, observed that the gait pattern of depressed patients differed qualitatively from that of normal controls. Walking in depressives was

characterized by a lifting motion, whereas normal subjects used a propelling motion, emanating as it were from the heel. This push-off appears to be absent in depressives: they move the leg forward, place the foot on the floor and then shift their weight, resulting in the so-called pulling gait.

Lemke (1985) compared the photographically recorded extension of the fingers of 23 normal right- and left-handed subjects with a group of eight psychotic depressed and schizophrenic patients. In the depressed patients the total extension and particularly the extension between thumb and index finger was restricted during the depression (201.5°) and increased after treatment (226.3°).

Summarizing, it can be concluded that by applying various measuring techniques on gross motor performance, a decrease in 24-hour activity and an increase of immobility were demonstrated in depressed patients. However, correlations between clinical and psychopathological variables proved to show little consistency. Actigraphic and related measuring techniques have offered few handles to get a better understanding of the nature of the retardation and the underlying mechanisms. The studies of hand and arm movements proper show that depressed patients are less able to accelerate these movements than normal controls and that they exhibit similar problems in simultaneous and sequential movements as reported in Parkinson patients.

VI. Fine motor behaviour

In 1989 a new measuring technique was introduced to quantify and analyse psychomotor retardation (Van Hoof et al., 1989): the recording of writing movements by means of a writing tablet (digitizer), a specially designed pen to measure pen pressure, and a personal computer (Maarse et al., 1988). This technique allows a simple, ecologically valid and highly accurate delineation of handwriting performance. The position of the pen on the digitizer is recorded with a frequency of 100 Hz and a precision of 0.2 mm. In addition axial pen pressure is recorded. In various studies implementing this technique a range of

tasks has been used simple motor tasks, like fast, repetitive up and down strokes (scratching), figure copying tasks of varying complexity (i e , the number of strokes per figure) and (perceptual and motoric) familiarity, the writing of the numbers 1 to 10 or of a brief text, and the computerized version of the Digit Symbol Substitution Test Accurate data of the various kinematic variables are obtained the total time as the sum of reaction time (RT) and movement time (MT), MT is further divided into movement time on paper (MTdown), including the time the pen is stationary on the paper, i e , pause time, and movement time above the paper, i e , while the pen is lifted (MTup) In some tasks the subject is able to recall the stimulus to the screen by touching with the pentip a red square on the digitizer, in which case MT also consists of video or reinspection time

In addition, the distance covered and movement speed per stroke are analysed, as well as information about the trajectory on and above the writing surface, and kinematic variables such as fluency, rhythmicity and accuracy of the movement These variables allow detailed analyses of the various cognitive and motor processes involved in the writing movements under investigation It is known that the larger proportion of reaction time is taken up by attentional and perceptual processes (detection, encoding and identification of the stimuli), the storing of this information in working memory and the planning of the next movement, the greater part of the movement time consists of motor processes involving visuo-motor programming, coordination, initiation and execution of the movement, feedback and the control of the feedback

In a first study of 20 depressed patients Van Hoof et al (1993, 1996) (Chapter 3) observed longer RTs and MTs on simple, and longer MTs on more complex figure copying tasks, compared to 20 controls Such complex figures were performed differently by the depressives and their reinspection times were also prolonged Of six patients a comparison between the performance before and after treatment with antidepressants could be analysed the changes on the HDRS correlated positively with the changes in RT and MT

Van Mier et al (1990) and Van Mier and Hulstijn (1993) compared 10 depressed patients, 10 patients with contusio cerebri (closed head injury CHI) and two groups of 10 matched controls each The patient groups exhibited longer RTs and MTs than the

controls. The greatest difference was constituted by the compensation strategies used; in addition the depressed patients made far more errors than the CHI-group and the stimulus reinspection intervals were longer. In Hulstijn et al. (1993; 1994) a group of 10 depressed patients was compared to as many controls in a variation on the Fitts task: two circles placed above each other were to be connected by a vertical stroke of approximately 10 mm; the task consisted of four sets of six trials. Patients were found to be slower in drawing the first line which, according to Hulstijn, could be attributed to problems in movement initiation as described by Widlöcher.

Sabbe et al. (1996a, b and 1997, and submitted) are currently replicating the findings mentioned above in larger groups of patients and further exploring the differences before, during and after treatment with antidepressants (fluoxetine: Prozac-R). Van Hoof et al. (in prep.) and Hulstijn (1996) are investigating the specificity of the data by comparing them to the results found in schizophrenics, patients treated with different kinds of psycholeptics (Scheres et al., in prep.) and patients suffering from Parkinson's disease. With respect to the latter group, this study is in line with the work of Cools et al. (1984; 1990) concerning the reduced shifting aptitude and the reduced motor and cognitive shift performance of Parkinson patients.

Conclusions

This review of the literature summarizes the major findings of the research on the various psychomotor variables, more in particular non-verbal behaviour, speech, reaction time, gross and fine motor performance, since the review article by Greden and Carroll (1981). In their conclusions, Greden and Carroll at the time put great faith in EMG measurements of facial expressions and on further studies of speech. These EMG measurements seem to have ended in a cul-de-sac, whereas the research of speech has

expanded considerably and, aided by computerization, has led to the identification of a large number of variables with regard to psychomotor retardation and has resulted in the determination of correlations with clinical parameters of depression and those of improvement during and after treatment (Kuny and Stassen, 1993). However, the selection of relevant variables remains a problem (Nilsonne, 1987 and 1988).

In the same period other developments have proved their significance. The SRRS was validated in large subject groups and has been used in many studies. The Core-system was developed and used to measure psychomotor signs particularly in melancholic and psychotic depression. The observation, classification and analysis of specific types of non-verbal behaviour were enhanced and differentiated. In choice reaction time tasks choice or decision time (DT) and movement time (MT) were measured separately, and cognitive complexity was manipulated: in depressed patients longer DTs and MTs were found; after improvement only a decrease in DT was observed. Actigraphic studies demonstrated a drop in activity and an increase of immobility during depression; circadian variations could be reliably proved; especially the immobility measure proved a valuable index of clinical improvement; indications were found that a motor deficit persists after recovery from depression.

We see the introduction of the recording and analysis of writing and drawing movements as an asset for this entire field of research. This uncomplicated method makes a reliable study of an ecologically valid skill possible; in contrast with speech studies, the number of variables is limited; there is a thorough knowledge of the cognitive and motor processes that determine this behaviour; and finally, both the cognitive and motor complexities can be manipulated independently.

In general it can be said that most studies using the various measuring techniques showed that, as a group, depressed patients were slower than normal, healthy control subjects. This retardation proved to be -either partially or entirely- of a cognitive nature. Whether motor retardation also occurs is less clear. In most studies in which the effects of treatment with antidepressants or electroconvulsive therapy were measured, a decrease in slowing was demonstrated after treatment.

If a further computerization of the applied measuring techniques is forthcoming, and if these techniques are safe, non-invasive and relatively reliable and cheap in comparison with the high-tech approaches such as PET, SPECT, MRI (Greden, 1993), their application will in all likelihood increase. In this respect the recommendations made by Greden and Carroll (1981) and Greden (1993) still hold: a careful diagnosis and classification of selected (sub) groups, within-patient-designs, control of variables such as age, sex, the use of medication, alcohol and drugs, and chronobiological factors such as circadian elements and seasonal influences. The combined application of various measuring techniques (e.g. to record writing and eye movements), and the linking of these with neuro-imaging techniques will hopefully lead to a considerably deeper insight into psychomotor retardation. The study of the use, by both normal and depressed patients, of various types of psycholeptics whose effects are known, might also make a valuable contribution to this understanding.

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FIGURE COPYING AND PSYCHOMOTOR RETARDATION IN DEPRESSION

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Abstract

Psychomotor retardation is one of the characteristic symptoms of a major depression. The purpose of this study was to examine the usefulness of a new methodology in the study of retardation. This methodology consisted of the computerized recording of pen-tip movements during figure copying tasks. It was found that, compared to controls, patients needed more time to complete the figure copying tasks and performed them in a different way: the patients lifted the pen more frequently, they paused for longer periods and they needed to reinspect the figure more often to copy it. The patients also needed relatively more time as the figure became more complex or less familiar. In a small number of patients, who were retested after therapy, the differences in motor activity between the first and second test correlated highly with clinical improvement. It is concluded that the methodology is suitable to gain more insight into the symptom of retardation and may be suited to obtain objective parameters to measure the effects of therapy.

One of the major features of a major depression is an overall slowness generally referred to as "psychomotor retardation". The symptoms cover a wide range of phenomena (see Benson, 1990; Widlöcher, 1983), among them a retardation or lack of proximal movements, such as a retarded gait, and a limited number of spontaneous movements of the head, trunk and arms. They include impoverished speech as well as restricted modulation of the voice. Symptoms such as lack of interest, easily induced fatigue and dysfunctions in memory and concentration are also classed among these phenomena. All these aspects are incorporated in scales that assess the severity of the depression, such as Zung's Self-rating Depression Scale, the Montgomery Asberg Depression Rating Scale and the Hamilton Depression Rating Scale, which are viewed as reliable indicators of depression (Widlöcher, 1983). Hence, motor retardation is seen as one of the central features of a "Major Depressive Episode" (DSM-III-R; American Psychiatric Association, 1987).

Psychomotor retardation is generally regarded as a secondary symptom, subordinate to mood disturbance. Widlöcher (1983), however, favours a primary role for psychomotor retardation. One of his arguments is that retardation not only is one of the most common symptoms, but that, in a number of factor analytic studies of depression rating scales, it also explains a larger proportion of the variance than depressive mood. Retardation also proved to be one of the best predictors of a positive response to tricyclic antidepressants (Bielski & Friedel, 1976). This is why Widlöcher considers retardation to be a "primary disorder in a depressive condition" (Widlöcher, 1983).

Even if the primary role of retardation in depression is not acknowledged, it still remains an important symptom. Indeed, this symptom can be measured more objectively than for instance a patient's affective state or feelings. Apart from the importance of measuring retardation to establish the severity of the depression, it can also facilitate the diagnosis of subgroups, e.g. to differentiate between retardation and agitation. In addition,

retardation can be used as an objective indicator of the course of the illness and finally, as mentioned above, it could serve as one of the predictors of the effects of treatment.

Various methods have been applied to assess psychomotor retardation (for an overview see Greden and Carroll, 1981). One method consists of the observation of the clinical manifestations of psychomotor retardation and its scoring on a rating scale (Widlöcher, 1983), another of the analysis and scoring of video recordings (Ulrich & Harms, 1985; Bouhuys et al., 1991). Although these methods provide a clear description of some categories of retardation, they are not sufficiently objective and very time consuming.

An entirely different approach entails the measuring of motor activity over a longer period by means of special equipment that records limb movements (Royant-Parola et al., 1986). These recordings give a general indication of mobility and immobility, which can be reliably related to the sleep-wake cycle. However, the recordings do not allow a differentiation of specific components of retardation like cognitive or pure motor aspects.

A third approach to the assessment of retardation involves tasks in which reaction times of subjects are measured in an experimental set-up. Usually, reaction time is subdivided into decision and movement time, which allows a distinction between the cognitive and motor components of retardation. Both appear to play a part in depression (Widlöcher & Ghozlan, 1989). A disadvantage of these tasks is that rather unusual and unnatural behaviour is studied, requiring highly motivated subjects.

A fourth approach consists of the recording and subsequent quantification of more natural behaviour. A number of studies has focused on speech. When subjects are requested to count from one to ten, the pauses during counting are found to be longer in depressed patients (see Greden and Carroll, 1981; Szabadi et al., 1976).

The method introduced in this article concerns the recording of pen-tip movements in writing and drawing tasks. In recent years the motor and cognitive aspects of writing and drawing have been studied intensively (for an overview see Thomassen and Van Galen, 1992). With the aid of a digitizer, a kind of electronic graphics tablet, pen-tip movements can be stored in a computer (Teulings & Maarse, 1984). This technique allows the measurement of a number of kinematic variables such as velocity, acceleration, pen point-

pressure and the fluency of movements, even of small strokes. In addition, reaction time and the duration of the movements can be measured separately. The duration of pauses between successive movements can also be determined. The tasks the subject is submitted to can range from typical laboratory tasks to reasonably natural ones. Moreover, the tasks can be varied in several dimensions, e.g. the motor or cognitive demands made on the subject can be increased (Hulstijn & Mulder, 1986; Hulstijn & Van Galen, 1988; Van Mier & Hulstijn, 1993). Thus, the study of writing and drawing combines a number of the positive features of the earlier approaches.

The present study was designed as a first test of the usefulness of this new approach. Writing and drawing movements were measured using two variants of one figure copying task. In line with the stimulus-reaction tasks as employed by others (Van Mier & Hulstijn, 1993) this study also focuses on the copying of line drawings and letters. Reaction time, movement time and pen pressure were measured separately. The aim of our study was to test whether depressed patients would be slower in performing these tasks than control subjects and to examine whether either reaction time or movement time would show the largest differences between patients and controls. Secondly, the effects of the manipulation of cognitive task variables were studied by varying the degree of complexity and familiarity of the stimuli in the copying tasks. Finally, in a limited number of patients we examined whether clinical changes would be reflected in the performance of these copying tasks.

Subjects and design

Two studies were carried out, each with 10 depressed patients (both patient groups consisted of eight women and two men, with a mean age of 54.7 and 43.4, respectively) and 10 healthy control subjects matched for sex, age and education. In the first study all patients were tested at the start of clinical treatment and six patients were retested at the end of their therapy (after two to three months). In the second study all patients were tested during their clinical treatment.

The patients were treated at the Department of Psychiatry of the University Hospital Nijmegen (Academisch Ziekenhuis Nijmegen). All patients met the DSM-III-R criteria for a Major Depressive Episode (American Psychiatric Association, 1987). All fell in the category of the unipolar subtype and were in different stages of the illness. For the purpose of diagnosis and to exclude other disorders, the patients were interviewed and underwent a general and neurological examination as well as a number of lab tests. In both test sessions the patients were tested while taking conventional medication: overall 150 mg of tricyclic antidepressants, amitriptyline or clomipramine. Four of the twenty patients (and one of the retested patients) also took low dosages of neuroleptics. The medication regime was not altered during treatment.

Recording

The pen-tip movements during writing and drawing were recorded with a Calcomp 2300 digitizer and a personal computer. The subjects were asked to copy the figures shown on a monitor placed in front of them. The presentation of a figure was indicated by two auditory signals. The subjects were instructed to copy the figures as fast and as accurately as possible on a sheet of paper placed on the digitizer. A specially designed pen was used

(Maarse et al., 1988), allowing pen pressure to be recorded. The writing stylus resembled an ordinary ballpoint pen, but was connected to the digitizer via a thin wire. The pen-point position was sampled with a precision of 0.1 mm at a rate of 100 Hz. As soon as the subjects had completed the copying of the figure presented to them, a wide range of movement characteristics could be analysed.

In this study the following variables were examined: total drawing time (TT) subdivided into reaction time (RT), i.e., the time interval between the presentation of the stimulus and the start of the first drawing movement, and movement time (MT), i.e., the time between the start of the first and the completion of the final drawing movement. Movement time was subsequently divided into the time the pen was above the paper (movement time "up", MTup) and the time the pen was on the paper and pen pressure exceeded 24 g (movement time "down", MTdown). As soon as the subject started drawing, i.e., when pen pressure exceeded the threshold level, the stimulus figure disappeared from the screen. In the second task (task B) the subject was able to recall the stimulus figure to the screen by moving the pen to a small red square (2 x 2 cm) at the bottom right of the drawing surface on the digitizer and touching it. However, as soon as drawing was resumed, the stimulus disappeared again. The subject was asked to use this opportunity for reinspection as little as possible, limiting it to prevent major errors. The duration of these reinspection intervals (Video time) was also recorded.

Drawing tasks

Two drawing tasks were used, a simple task (A) and a more complex task (B) (see Figure 1). In task A one of six stimulus figures was shown on the screen placed in front of the subject, each figure six times in a random order. In order to examine the effects of an increase in complexity of the tasks on performance, in task A the copying performances of stimuli 3 and 5 were compared with the performances of the more complex stimuli 4 and 6.

In task B three categories of stimuli were presented. The factor complexity was manipulated by an increase in the number of strokes from 4 to 8 (see Figure 1). The factor familiarity was studied by decreasing the familiarity of the stimuli in these three categories. The first category consisted of letters, stimuli both perceptually and motorically familiar. The second category was made up of familiar figures, stimuli that are motorically unpractised, but perceptually familiar. Figures like an arrow and table were placed in this category. All symbols and objects were familiar. The third category consisted of unfamiliar figures: stimuli that were both perceptually and motorically unfamiliar. The figures in this category were meaningless patterns, of which is assumed that they, compared to the familiar figures of the previous category, would require more time as far as perceptual processing and movement planning are concerned.

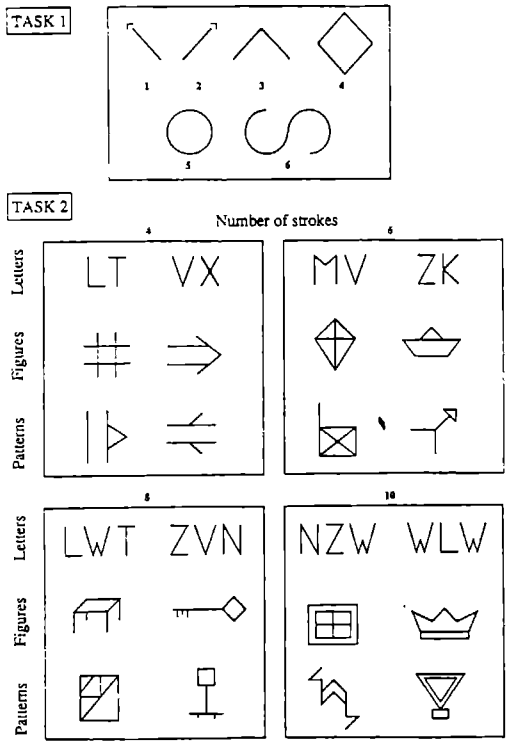

Figure 1. The stimulus figures of task A and task B.

Depression Rating Scales

The severity of the depression in the patient groups was established by the Hamilton Depression Rating Scale (Hamilton, 1960) and the Montgomery Asberg Depression Rating Scale (Montgomery & Asberg, 1979). In addition, patients filled in the Zung Self-rating Depression Scale (Zung, 1965). The Salpêtrière Retardation Rating Scale (Widlöcher, 1983) was also employed. This scale was specifically designed to measure the clinical severity of retardation.

Neuropsychological tests

Furthermore, three of the most frequently used neuropsychological tests were applied. Firstly, the Fifteen-words Test for verbal memory (Deelman, 1972), in which the subjects are requested to memorize and repeat a list of 15 words, which is repeated five times. The score used consisted of the number of correctly reproduced words of all five repetitions combined. The second test was the Stroop Test (Jensen & Rowler, 1966) which measures aspects of attention. Finally, a fluency task (Ekström et al., 1976) was administered. In this test the subjects have 60 seconds in which to produce as many words of a certain category as they can.

Procedure

All tests were administered in the afternoon. The subjects were tested in a quiet room in the Department of Psychiatry. The total session took approximately one hour.

Statistical analysis

For each dependent variable an analysis of variance was conducted using a mixed design with the group difference and the difference between patients and controls as between-

subject factors, and the complexity in task A and complexity and familiarity in task B as within-subject factors. In order to study the effect of the factor complexity within tasks A and B, a comparison was also made between the performances on the copying of the figures $\wedge$ $\circ$ and $\diamond \omega$ (task A), and between the performances in the copying task of figures with either four or eight strokes (task B). To examine the effect of the factor familiarity within task B, a comparison was made between the performances in the letter copying task and the copying of figures and unfamiliar patterns.

Results

Table 1 depicts the means and standard deviations of the scores on the depression scales, the neuropsychological tests and the performance on the drawing tasks during the first session. Group differences were analysed with a t-test. In the table the observed significance levels are presented.

Table 1 Means and standard deviations of patients and controls of the scores on the depression scales, neuropsychological tests and copying tasks of the first test session TT Total drawing time, RT reaction time, MT movement time, MTup movement time above the paper, MTdown movement time on paper, Video time reinspection time

Test	Group				p		
	patients		controls		group	group * complexity	group * familiarity
	mean	SD	mean	SD			
Hamilton	22 55	6 12					
ZUNG	59 84	8 49					

MADRS	27 88	6 63					
Salpêtrière	24 85	9 14					
Fluency	17 22	5 85	26 40	9 90	<0 05		
Stroop III-II	54 58	35 43	33 30	10 60	<0 05		
15 words	40 21	9 02	42 70	8 43	ns		
Task A							
TT	3 46	1 24	2 41	0 94	0 005	0 003	
RT	1 50	0 59	0 96	0 27	0 001	0 039	
MT	1 96	0 80	1 45	0 71	0 039	0 019	
MTup	0 37	0 65	0 20	0 25	0 146	0 195	
MTdown	1 59	0 45	1 25	0 62	0 098	0 021	
Task B							
TT	9 48	3 90	6 61	2 51	0 013	0 033	0 032
RT	2 77	1 65	2 13	1 81	0 188	0 276	0 317
MT	6 72	2 83	4 48	1 53	0 007	0 067	0 021
MTup	2 13	0 70	1 50	0 62	0 007	0 365	0 542
MTdown	3 23	1 56	2 45	1 02	0 086	0 859	0 019
Video time	1 35	1 23	0 53	0 49	0 015	0 091	0 071

The scores on the depression scales show that the patients were moderately depressed and retarded (the cut-off score for the Salpêtrière Retardation Rating Scale is 20; Widlöcher, 1983).

Two of the three neuropsychological tests yielded significant differences between patients and controls. Patients produced significantly fewer words in the fluency task and scored significantly lower on the Stroop Test.

The performances on the drawing tasks demonstrate that the total drawing time (TT) of patients was longer than that of the controls in both tasks. In the simple task (A) both reaction time (RT) and movement time (MT) were significantly prolonged in patients. In the more complex task (B) only movement time (MT) and reinspection time (Video time) were significantly longer. There were no significant differences in reaction time.

What is most notable in the latter (more complex) task is that the prolonged MT can for the greater part be attributed to longer movement times above the paper (MTup), i.e., the pause intervals. In task A as well as in task B an increasing complexity within the task led to a relatively longer total drawing time in patients. In task A a relatively prolonged reaction time and movement time were obtained. In task B there was only an (almost significant) increase in movement time. A similar profile emerges with respect to the effects of decrease in familiarity. Here, too, total movement time, and not reaction time, was found to be longer. However, it is remarkable that this increase in movement time is, in this instance, found to be the result of a lengthening of the time the pen was on the paper (MTdown).

In order to make a comparison between the performances on the drawing tasks at the beginning of clinical treatment and at the end of treatment, six patients from the first study were tested twice. (Of the remaining four patients two had already left the hospital before they could be retested; with the other two patients medication had been changed in the meantime). Of these six patients two had deteriorated scores on the depression rating scales, which was also reflected in a poorer performance on the drawing tasks. Two patients improved substantially and two recovered completely. The changes on the

Hamilton scale correlated significantly (0.73 or higher) with changes in reaction time and movement time in task A and with changes in movement time in task B.

Discussion

The depressed patients were slower on a large proportion of the movement variables of both drawing tasks. These findings, and the general impression during testing, suggest that the recording and analysis of the execution of drawing tasks might well be a valuable contribution to the existing methods to measure psychomotor retardation in depressed patients.

One of the present study's objectives was to examine which variable would show the largest group difference. In the complex task B significant differences were found in movement time (MT), particularly for those intervals the pen was above the writing surface (MTup), i.e., the pauses. These findings are in agreement with findings in earlier speech studies: the largest group differences were not observed in the actual duration of the "motor" execution - phonation time -, but in the silent intervals between the audible segments of speech (Szabadi et al., 1976; Greden & Carroll, 1981). This suggests a slowing in the planning and preparation of the movement.

In line with these findings is the fact that the factors complexity and unfamiliarity of the stimulus had a larger effect on the performance of the depressed patient group than on the control subjects. These results indicate that in the figures used in this study the cognitive processes mainly account for the observed retardation rather than the motor aspects of the execution. Our recent study (Sabbe et al., 1996) shows that, in addition to a "cognitive" slowing, a clear "motor" slowing is also found to exist.

Reaction times of the patients differed significantly from those of the controls in the simple task (A) only; no differences were observed in the complex task (B). This finding

seems to be at variance with the earlier findings of prolonged reaction times in all tasks (Martin & Rees, 1966; Byrne, 1976; Cornell et al., 1984; Knott & Lapierre, 1987). A possible explanation for this discrepancy is that the complex task (task B) used in this study was considerably more difficult than the rather simple tasks employed in these earlier studies. Task B may have been too difficult for a number of patients. For one, they made more errors (43% in patients against 14% in controls). Moreover, the patients seemed unable to memorize all relevant features of the complex stimulus figures during the reaction time interval. They started drawing somewhat too quickly and could only draw a part of the figure before they had to re-inspect the stimulus in order to complete it. It is probable that they used a different strategy than the controls. The controls tried to copy the entire figure without reinspection and as a result needed relatively more time before they could initiate the drawing movement. This explanation is in line with the observation that depressed patients often use a more detailed, more sequential and intentional mode of operation, which can be interpreted as a manifestation of the dysfunctioning right hemisphere (Weingartner & Silberman, 1984). Possibly, depressives experience more difficulties with tasks that require a "holistic" or "gestalt" approach and since they fail, they are more inclined to opt for a serial strategy. This strategy is assumed to be mediated by the left hemisphere. According to this view depression can be explained by the fact that the already maximally activated and partially failing left hemisphere makes an ineffective demand on the impaired right hemisphere. Weingartner and Silberman (1984) mention a number of studies that support this viewpoint: the findings of studies on lateral eye movements (Ahern & Schwartz, 1979), electroencephalography (Davidson et al., 1979) and dichotic listening (Yozawitz et al., 1979). The outlined hypothesis offers an explanation for both the lack of a significant difference in reaction times between patients and controls in task B and for the significantly prolonged reinspection intervals. Our finding that patients experience more difficulties with the more complex and less familiar figures and patterns is also in agreement with this theory.

An alternative hypothesis suggests that letters are produced more or less automatically since they are perceptually and motorically overlearned. This would explain why

depressed patients encounter fewer problems in the execution of "automatic" tasks. This theory is also widely supported in the literature (see e.g. Byrne et al., 1986; Tancer et al., 1990).

Overall, the results of the neuropsychological tests were in line with the findings in the copying tasks. In the fluency task patients produced far fewer words than the controls. The performance of patients on the Stroop test was also inferior. The Fifteen-words test, however, did not generate any significant differences. The latter result is in contrast with findings of earlier studies in which memory tasks showed poorer performances in depressed patients (Cohen et al., 1982; Brand, 1987; Golinkoff & Sweeney, 1989; Tancer et al., 1990). A possible reason for this discrepancy could be that an inferior performance is only observed in patients suffering from a severe depression and not in mildly depressed patients, who constituted the patient group in the present study. In our study the mean Hamilton score was lower than the reported scores in these earlier studies.

Four of the twenty patients were treated with neuroleptics. These neuroleptics may have had an effect on the writing and copying performance. King (1990) comments that the effects of neuroleptics on psychomotor functions are inconsistent and show a large between-subject variability. In our study this effect is likely to have been rather small since it only concerned four of the twenty patients and no extrapyramidal symptomatology was established in clinical examinations. As regards the use of antidepressants: the patients were tested while they were on conventional medication, which could account for the observed retardation in the copying tasks. However, Deptula and Pomara (1990) point out that in most studies relating to this subject no significant effects on psychomotor performance were found. Another limitation of the present study is that only small groups of patients were tested. Although it cannot be excluded that other factors may explain the retardation observed in this study, we conclude as yet that the retardation can be mainly attributed to the depression and not to any medication, all the more since in a follow-up study by Sabbe et al. (1996), in which a larger number of patients is tested and in which the effects of medication are controlled, our findings are being replicated.

To what extent is the observed retardation specific for patients suffering from a major depression? In the literature only very limited data on findings in other patient groups are available. Our patients do differ markedly from patients with a psycho-organic syndrome (Van Mier et al., 1992). Our current study also includes schizophrenic patients. The first results indicate that these patients exhibit a different movement pattern (Van Hoof et al., 1995).

In addition to further research into the specificity of our findings, an objective for future studies could be the investigation of the possibilities the described method offers to measure the effects of therapy. The high correlations between the improved scores on the Hamilton scale and the changes in reaction and movement time observed in the present study look very promising.

Since the introduction of the digitizer, allowing the very accurate recording and analysis of kinematic variables of pen-tip movements, the research into the motor aspects of writing and drawing has expanded considerably (for an overview of the literature see Thomassen and Van Galen, 1992). The study presented here is the first applied study of its kind into issues relating to the assessment of the nature of psychomotor retardation in depression.

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FINE MOTOR RETARDATION AND DEPRESSION

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Abstract

New computerised techniques allow the precise measurement of psychomotor retardation in patients with a Major Depressive Episode (MDE). One such a technique is the analysis of writing and drawing behaviour during figure copying tasks. In the present study, 22 inpatients with an MDE were compared to 22 normal controls. Three tasks were used: the drawing of lines and simple figures, the copying of complex figures and a task in which figures had to be rotated. Objectives were to provide support for earlier findings that the patients were slower than the controls and to explore the cognitive and motor processes involved. Two strategies were applied: analysis of the reaction time and movement time and their different components, and manipulation of the cognitive and motor demands. Patients showed considerable retardation on most of the kinematic variables. Motor deficits and cognitive slowing contributed to this retardation. Cognitive difficulties increased with increasing complexity of the task.

Although changes in psychomotor activity are generally viewed as important phenomena, their contribution to the diagnostic and therapeutic evaluation of patients with affective disorders remains unclear. Firstly, some authors consider psychomotor alterations to be an important symptom - on the same level as other symptoms (DSM) -or even as a core symptom of all depressive conditions or some subgroups. Secondly, a number of psychomotor symptoms have been grouped into a syndrome with its own etiology, pathogenesis and psychoneurophysiology, comparable with fever, as an independent syndrome in different physical conditions. The "akinetic syndrome" (Bermanzohn & Siris, 1992) and the "psychotic motor syndrome" (Günther et al., 1985) are examples of this way of thinking. This syndrome can be present in different neuropsychiatric disorders, such as Parkinson's syndrome, retarded depression and schizophrenia, but also in pharmaceutical intoxication and in association with aging. Thirdly, some investigators consider psychomotor retardation as a primary disorder in depression (Widlöcher, 1983): it can explain a large proportion of the variance in depressive symptomatology, it offers new insights into the etiology of depression and it has predictive value regarding the therapeutic effects of antidepressive medication. These differences in opinion about the contribution of psychomotor retardation to the diagnostic process in affective disorders, are partly due to different operationalisations. The use of fairly "narrow" definitions means that only the motor behaviour manifested in facial expression, speech, gross and fine motor activity is taken into account. "Wider" definitions not only encompass motor behaviour, but also mental activities, e.g. disturbances of attention, memory and the experience of time, hedonia and vital functions such as sleep, eating behaviour and sexual libido. In the latter definitions, the underlying assumption stresses that retardation determines both motor and mental behaviour. To define psychomotor retardation more accurately, video-analysis of the non-verbal behaviour of depressed patients and analysis

of the perceptions of the clinician and their different weights in the diagnostic process (Ulrich & Harms, 1985) offer new research possibilities.

During the past decade and since the review article by Greden & Carroll (1981), new computerised techniques have been developed to measure psychomotor retardation (Greden, 1993). They focus on ecologically valid skills, such as speech and writing behaviour. In comparison with older methods such as rating scales (e.g. the Salpêtrière Retardation Rating Scale), actometry and choice reaction time tasks, they allow the more precise measurement and more detailed analysis of retardation. Furthermore they offer new scope to understand the different cognitive and motor processes involved in psychomotor retardation and to detect differences between the retardation of depressed patients and patients suffering from other neurological and psychiatric conditions. In the field of speech analysis, research is steadily increasing; several prominent features of speaking behaviour and voice sound characteristics were found to be closely related with depression and the time course of recovery (Kuny & Stassen, 1993; Flint et al., 1993). We introduced (Van Hoof et al., 1989) an innovative technique that consists of recording and analysing writing and drawing movements, e.g. in figure copying tasks. Figure copying tasks have been used as a diagnostic tool for the assessment of psychomotor dysfunction for more than half a century. They are sensitive indicators of a wide range of neurological disorders (Lezak, 1983) and are included in a large number of tests [see Van Mier (1992) for a list of eighteen tests]. Recording drawing movements during figure copying will improve our understanding of the sensory and motor processes involved in psychomotor retardation. These include a number of perceptual processes (preprocessing, feature extraction and stimulus identification), storage in the working memory, visuo-spatial processing and planning the next movement. These processes, which we refer to as cognitive, will take by far the largest portion of the reaction time (i.e., the time interval between the onset of stimulus presentation and the start of drawing). The other processes, denoted by the term "motor", encompass the programming, coordination, initiation and execution of muscle commands, as well as monitoring the visual feedback to correct errors. During movements, successive strokes are likely to be planned and programmed.

Motor processes therefore consume a small part of the reaction time and most of the movement time.

In line with two earlier investigations (Van Mier & Hulstijn, 1993; Van Hoof et al., 1993) this study compared a large group of patients with a Major Depressive Episode to a group of normal matched controls, in an attempt to replicate earlier results and to further explore the nature of depressive retardation. Therefore, the different components of drawing movements were analysed and in subsequent tasks, cognitive and motor variables were manipulated independently. The study questions were:(a) Are depressed patients slower in accomplishing different drawing tasks than normal controls?, (b) If so, in which aspects (kinematic variables such as the reaction time and movement time and their components) does psychomotor retardation manifest itself most prominently? (c) If the more cognitive demands and the more motor demands - insofar as they can be separated - are manipulated independently, on what points do depressed patients fail?

Method

Subjects

Forty-four subjects participated in the study: twenty-two patients with a Major Depressive Episode (MDE) and twenty-two control subjects. At the time of the study, all the MDE-patients were hospitalized at the Clinic of Psychiatry of the University Hospital Nijmegen, the Netherlands. The diagnosis was made after an extensive and detailed auto- and hetero-anamnestic interview. All the patients aged between 18 and 65 years with an MDE and a minimum score on the Hamilton Depression Rating Scale of 18, who were admitted between September 1992 and April 1994, were asked for informed consent after the nature of the procedure had been fully explained. Patients were excluded if they met one

of the following exclusion criteria: motor disabilities affecting writing behaviour (N=2), severe cardiovascular or hepatic disease (N=2), renal failure and previous unsuccessful treatment with fluoxetine (N=4). Consequently in total 8 patients were excluded; from a psychiatric point of view they did not differ from the sample. The group that participated in the study comprised twelve male and ten female patients. All the patients had a DSM III-R diagnosis of a Major Depressive Episode, single episode (296.2) or recurrent (296.3); only 1 patient had a Bipolar Disorder, Depressed (296.5). The episode was severe, in all the patients; sixteen of them did not have any psychotic features (code 3) and six did have psychotic features (code 4). Two patients had a subsidiary diagnosis of previous alcohol and benzodiazepine dependence (n=2). Three patients displayed a clinical state of agitation.

For each patient there was a control subject, matched for age, sex and education.

Procedure and tasks

Once admitted to the study, all antidepressant drugs were gradually stopped and other psychotropic drugs were slowly reduced as much as the condition of the patient allowed. Patients remained on low doses of benzodiazepines (N=11), neuroleptics (N=2) or a combination of the two (N=5). Then fluoxetine 20 mg a day was administered for six weeks. The test was performed after 1 week of fluoxetine. It consisted of a series of copying tasks with the aid of a pen on a digitising tablet. The movement registration method is discussed in the next paragraph.

Stimuli differed in complexity and familiarity (Figure 1). Complexity was defined as the number of strokes in a figure; familiarity could be perceptual or motor: letters e.g. are well-known perceptually and motorically, while figures such as a boat or a table are well-known perceptually but not motorically; novel and nonsense patterns are unknown perceptually and motorically.

Three copying tasks were assigned:

- Task I analysed whether retardation could be detected in the drawing of simple lines or whether more complex patterns were needed. The subjects had to copy 4 straight lines (one vertical, one horizontal and two diagonals) and 4 simple figures (Figure 1). All the stimuli were presented six times in a random order.
- The degree of complexity of the figures was increased in task II to answer the second and the third questions. Three types of stimuli had to be copied: combinations of capital letters, familiar figures and novel, nonsense patterns (Figure 1). Four stimuli of each type were presented with differing complexity, two with 4 strokes and two with 8 strokes.
- In task III a specific type of manipulation was executed that focussed on visuo-spatial processing. Eight figures, 4 combinations of letters and 4 figures (Figure 1) were presented, with the instruction to copy them at another angle, i.c. having rotated them through 90 degrees to the right.

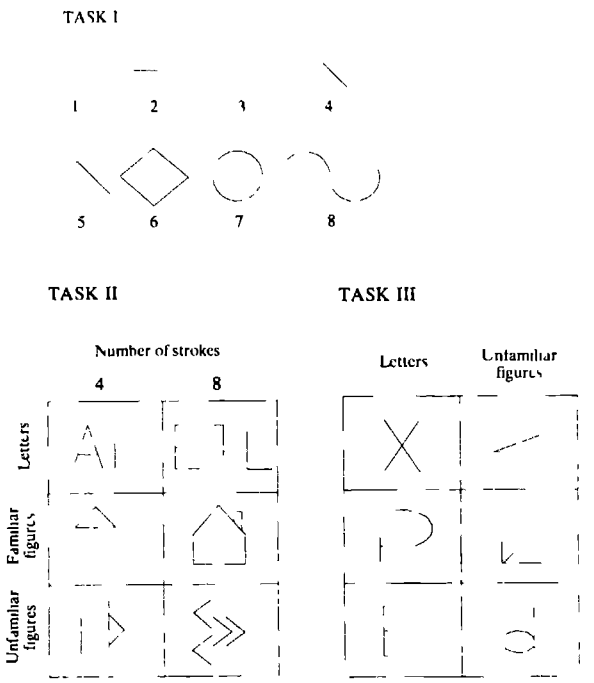

Figure 1. Stimulus designs used in Tasks I, II and III

In all the tasks, the subjects were instructed to draw as quickly and as accurately as possible. As soon as the pen touched the paper, the stimulus disappeared from the viewing screen. In tasks II and III, the subject could reinspect the figure by touching the pen on a red spot at the lower right hand corner of the digitiser. He/she was asked to do this only as an "emergency" measure, if he/she felt that otherwise too many errors would be made. Prior to each task, a practice session was given in which the subject could become accustomed to the writing tablet and the procedure. The investigators were independent of the treatment staff. The three tasks were performed in a fixed order in 30 to 60 minutes. They all took place between two and five p.m., to avoid possible influences of circadian rhythm.

Recording and analysis

The drawing movements were recorded using a Calcomp 2300 digitiser, connected to a PC (63S386) that had been specially designed to measure pen pressure, with a precision of 2 g (Maarse et al., 1988). The position of the pen on the digitizing tablet (axial pen force) was recorded with a frequency of 100 Hz and a precision of 0.2 mm. The following movement variables were obtained: total time (TT) i.e., the sum of the reaction time and the movement time; reaction time (RT), defined as the time interval between the onset of the stimulus presentation and the moment the pen touched the paper and the pressure threshold was exceeded; movement time (MT), i.e., the time interval between the first and last moment that the pressure threshold was exceeded. Movement time (MT) was divided into the time that the pen was moving on the paper and the pressure threshold was exceeded (MTdown), the time that the pen was on the paper but not moving (no velocity) (Pause), the time that the pen was above the paper and the pressure was below the threshold (MTup) and the video reinspection time (Video), i.e., the time that the figure was reinspected.

In task II and task III, the drawings were scored for errors by two independent investigators. The classification was as follows:

- A-type error: the drawing more or less resembled the actual stimulus. Distinction was made between small and severe errors:
  - A1: rotation error of up to 30°, distortion in proportion or in relation, segmentation of parts of the stimulus, fragmentation and alignment, omissions and additions (all up to 1/3 of the number of strokes of the original stimulus); also the drawings in which corrections had been made.
  - A2: rotation of more than 30°; two-dimensionality instead of three-dimensionality; wrong letter(s); omissions, additions, reversal and distortion in form (all up to 2/3 of the number of strokes of the original stimulus).
- B-type error: the original stimulus could not be recognized because of too many omissions or additions, or no copy had been made.

Statistical analysis was performed with two-way ANOVAs for each variable according to a repeated measurement design. The within factors were complexity (Task I), complexity and familiarity (Task II), and familiarity (Task III), while the between factor was group (patients versus controls).

Results

Task I: Lines and simple figures

Even during the line drawing task the mean reaction time (961 msec) and the mean movement time of the patients (600 msec) were significantly longer than those of the control group (758 msec and 421 msec respectively) (Figure 2). Table 1 presents the results of the ANOVA for total time (TT), reaction time (RT), movement time (MT),

movement time pen up (MTup), movement time pen down (MTdown), pause time (Pause) and video reinspection time (Video) for tasks I, II and III.

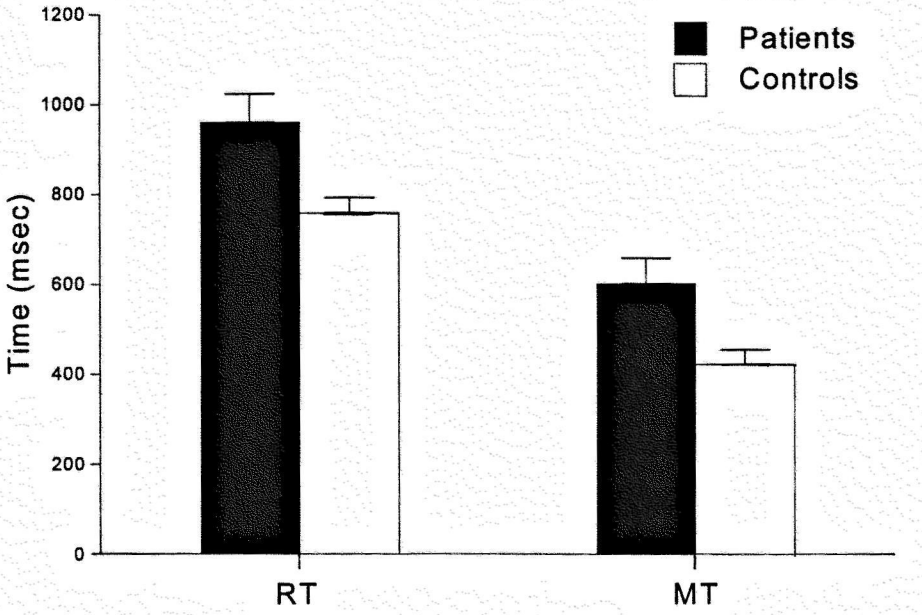

Figure 2. Mean reaction time (RT) and mean movement time (MT) of the depressed patients and their controls for copying lines in Task I

Table 1

Analysis of Variance for the Kinematic Variables of Tasks I, II and III

	df	TT	RT	MT	MTdown	MTup	Pause	Video
Task I (lines)								
Group	1	10 12**	8 09**	7 49**				
Task I (simple figures)								
Group (G)	1	7 54**	8 36**	4 38**				
Complexity (C)	1	100 06***	15 16***	221 63***				
G x C	1	7 73**	8 27**	4 59*				
Task II (complex figures)								
Group (G)	1	6 74*	4 81*	6 57*	5 12*	2 42	4 12*	5 37*
Familiarity (F)	2	46 52***	20 27**	24 51***	23 60***	7 12**	12 52***	8 33**
Complexity (C)	1	171 93***	53 92**	182 79**	191 98***	244 49***	28 03***	17 49***
G x F	2	1 13	0 17	1 19	3 05#	4 23*	0 75	1 44
G x C	1	5 55*	2 53	5 35*	3 02#	0 31	1 84	5 05*
G x F x C	2	2 51#	0 50	2 56#	9 90***	3 87*	3 27*	1 36
Task III (rotation)								
Group (G)	1	5 79*	3 66#	4 51*	0 59	4 51#	2 27	2 09
Familiarity (F)	1	42 60***	7 47**	5 76***	9 25**	44 26***	36 77***	38 24***
G x F	1	2 05	0 80	1 65	0 49	1 74	3 07#	1 39

Note F-values for total time (TT), reaction time (RT), movement time (MT), movement time pen down (MTdown), movement time pen up (MTup), pause time (Pause) and video reinspection time (Video)

#p< 10 *p< 05 **p< 01 ***p< 001

The mean reaction time and the mean movement time for copying the simple figures are presented in Figure 3.

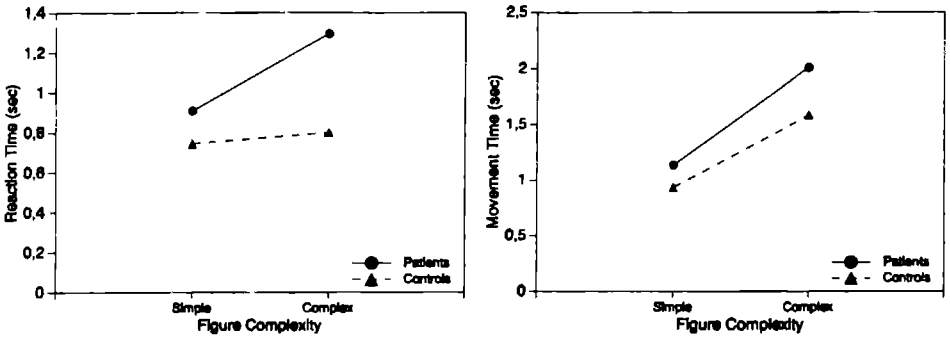

Figure 3. Mean reaction time (RT) (left panel) and mean movement time (MT) (right panel) of the depressed patients and their controls for copying simple figures in Task I

For all the figures, the depressed patients had a longer reaction time (mean RT patients: 1089 msec, mean controls: 789 msec) and a longer movement time (mean MT patients: 1559 msec, mean MT controls: 1258 msec) than the control subjects. The mean effect of complexity on the RT and MT was significant (p=O.OOO). The mean differences were larger for the more complex figures (spiral-diamond) than for the less complex figures (circle-angle), as demonstrated by the significant interactions between group and complexity (Table 1).

Task II: Complex stimuli

The following variables were analysed: total time, reaction time, movement time, movement time pen down, movement time pen up, pause time and video reinspection time; also the number and severity of the errors were scored. Figure 4 presents the mean reaction time and the mean movement time of the two groups for three categories of stimuli: letter combinations, familiar figures and unknown patterns. For the other variables, the patterns were very similar.

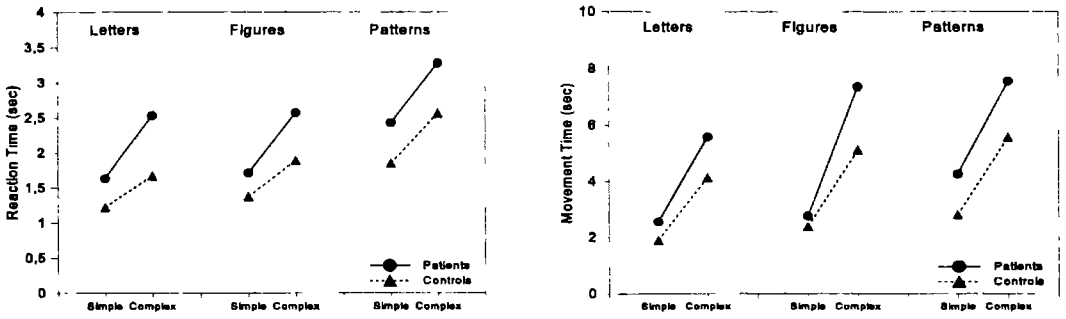

Figure 4. Mean reaction time (RT) (left panel) and mean movement time (MT) (right panel) of the patient group and control group for the three categories of stimuli of Task II: letter combinations, familiar figures and unknown patterns.

The depressed patients and control subjects differed significantly in the reaction time (mean RT patients 2358 msec, mean RT controls 1760 msec), the movement time (mean MT patients: 5012 msec, mean MT controls: 3653 msec), the movement time pen down (mean MT down patients: 2938 msec, mean MT down controls: 2228 msec), the pause time (mean Pause patients: 514 msec, mean Pause controls: 304 msec) and the video reinspection time (mean Video patients: 647 msec, mean Video controls: 231 msec). The difference in the mean pen-up movement time (mean MTup patients: 1426 msec, mean MTup controls: 1194 msec) was not significant (Table 1). It appears that the complexity affected the MTdown and the Video and that complexity and familiarity interacted with the MT, MTdown, MTup and Pause. Interaction effects between group and complexity/unfamiliarity were measured to find out whether increasing complexity/unfamiliarity had more effect on the patient group than on the control group. The following interaction effects were significant: group and complexity for MT, MTdown and Video; group and familiarity for MTup; group, familiarity and complexity for MT, MTdown, MTup and Pause. There was no difference in the number of errors or types of error between the two groups.

The mean reaction time (patients: 4038 msec, controls: 2312 msec) and the mean movement time (patients: 3132 msec, controls: 2312 msec) for copying the letters and the figures after clockwise rotation through 90 degrees, are presented in Figure 5.

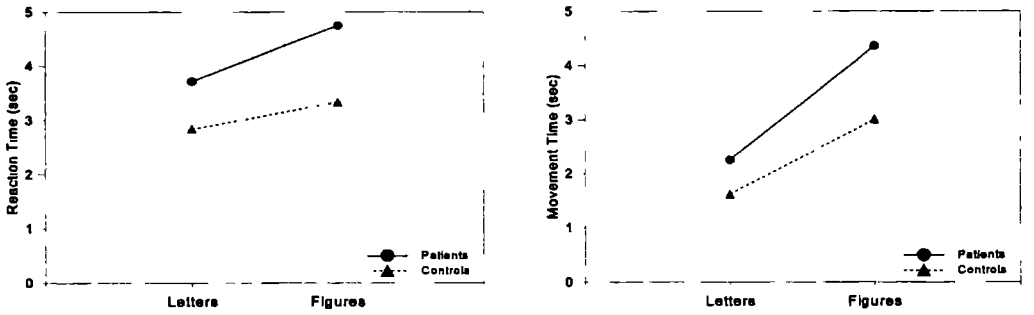

Figure 5. Mean reaction time (RT) (left panel) and mean movement time (MT) (right panel) of the patient group and control group for rotating the letters and figures of Task III

In general, the results were similar to those for task II: Not only the reaction time and the movement time, but also the movement time pen up, discriminated between the two groups (Table 1). There were no significant interaction effects between group and letter/figure familiarity, with the exception of a small effect for the pause time. There was no difference in the number of errors or types of error between the two groups.

Clinical Scales, Medication and Kinematic Variables

The mean score and standard deviation of the patient group on the Hamilton Depression Rating Scale was 24.4 $\pm$ 5.8, on the Zung Self-Rating Scale 59.2 $\pm$ 10.4, on the Salpêtrière Retardation Rating Scale 24.5 $\pm$ 7.2. Correlations were analysed between the results on these clinical scales, the use of neuroleptic or hypnotic medication and the values of the kinematic variables (Table 2). No correlations were found between the depression rating scales and the kinematic variables. The correlations between the

Salpêtrière Retardation Rating Scale and the kinematic variables were very low. Only one correlation was found between the use of co-medication and the kinematic variables. The use of neuroleptics correlated significantly with the movement time for copying the simple figures. Table 2 indicates the correlations between the results on the Hamilton Depression Rating Scale, the Zung Self Rating Scale, the Salpêtrière Retardation Rating Scale, the use of neuroleptic or hypnotic co-medication and the following kinematic variables: reaction time for tasks I, II and III; movement time for tasks I, II and III.

Table 2

Intercorrelations Between Clinical Scales, Medication and Kinematic Variables

	1	2	3	4	5	6	7	8	9	10	11
1 HDRS	--	47	39	- 21	31	- 06	- 19	- 12	- 09	04	08
2 Zung		--	30	11	34	07	35	03	21	26	33
3 Salp			--	14	07	37	29	15	23	19	13
4 Neur				--	05	- 06	45	- 16	- 09	- 08	- 22
5 Hyp					--	- 01	06	- 08	10	14	24
6 RT I						--	61	90	81	49	56
7 MT I							--	57	73	46	54
8 RT II								--	83	55	61
9 MT II									--	61	76
10 RT III										--	46
11 MT III											--

Note. Clinical scales HDRS = Hamilton Depression Rating Scale; Zung = Zung Self Rating Scale, Salp = Salpêtrière Retardation Rating Scale Use of medication Neur = neuroleptic medication, Hyp = hypnotic medication Kinematic variables· RT I, RT II, RT III = reaction time for Tasks I, II, III, MT I, MT II, MT III = movement time for Tasks I, II, III.

The depressed patients were much slower on most of the measures in the three drawing tasks, i.e., copying simple figures like a circle or a diamond, copying complex figures - letter combinations, familiar figures or unknown patterns - and rotating letters and figures. The depressed patients had significantly longer reaction times and movement times than the normal control subjects. Even when drawing very simple lines in different directions (horizontal, vertical and diagonal), the reaction and movement times of the patients differed significantly from those of the controls. When we considered the performance of individual patients, wide variation, and great inter-individual differences were found. Most of the patients were moderately slow, some of them were two to five times slower than the controls, some were not retarded or were even faster than their controls. Further studies are required to determine which factors are responsible for these differences and whether these findings are also applicable to outpatients and community samples. Although it is not certain whether the medication had a positive or negative effect, we do not consider this factor to be important. After consideration of all the variables in the three tasks, only one statistically significant correlation was found between the patient subgroups without and with different classes of medication and the kinematic variables. Studies on the psychomotor and cognitive effects of fluoxetine did not demonstrate any behavioural toxicity (Hindmarch, 1995), while another study demonstrated slight shortening of the reaction time in choice reaction time tasks after one week of treatment with this antidepressant (Kerr et al., 1993). The age range of our sample was fairly wide: 18 - 65 years. There were no correlations between age and the kinematic results in the patient and control groups. In line with earlier findings, there were only weak correlations between the scores on the Salpêtrière Retardation Rating Scale and the values of the kinematic variables. This reflects the difference between the measurement of a specific short-term motor act and the rating of general verbal and non-verbal information in a questionnaire (D. Widlöcher, personal communication, June 23, 1995).

In general, these results replicate the findings in the two earlier studies (Van Mier & Hulstijn, 1993; Van Hoof et al., 1993) and are of the same order of magnitude. This confirms the reliability of this method for studying psychomotor retardation.

Our second question: In which aspects of the fine motor behaviour does the retardation manifest itself the most prominently? required a detailed analysis of the different kinematic variables that determine psychomotor retardation. This involves cognitive processes (perceptual, visuo-spatial, storage and planning) and motor processes (programming, coordination, initiation and execution of the motor act). The reaction time could be considered to mainly reflect cognitive processing, while the movement time was largely determined by motor processing. We found that when drawing lines and simple figures (Task I) the reaction time and movement time of the depressed patients were longer than those of the controls; this also applied to copying the more complex figures (Task II). In this test, which involved the more complex figures, the movement duration of the patients was prolonged, because their pen was moving more slowly on the paper, their pauses on the paper were longer and they needed more and longer reinspections to copy the figure. They took more time before starting to draw, took longer pauses, drew more slowly and inspected the figure more often than their controls. The resulting drawings did not differ between the two groups: the patients did not make more errors than the controls. The results were similar for the rotation task (Task III): longer reaction and movement times, especially the pen up time, i.e., the duration that the pen was held above the paper.

All these results strongly suggest that depressive retardation, apparent in all the tasks from the simpliest to the most complex, has a double origin, cognitive and motor. This motor component, (reflected by prolongation of the movement duration and specifically by the pen-down time), was less apparent in the "classical" reaction time tasks, in which the motor component often consisted of moving towards a button and pressing it. This "Pure" motor retardation was also detected in our earlier work (Van Mier & Hulstijn, 1993; Van Hoof et al., 1993), but the pattern was slightly different. The patients did not have longer reaction times, but their movement times were prolonged because of longer pen-down times, pen-up times and video reinspection times. They also made more errors than the

control group. It would seem that when depressed patients are confronted with more complex figures, they have to choose between different strategies to cope with their difficulties. If they try to gain an overview of the whole task, their reaction will be slower and the execution of any movements will be slower, with more pauses while the pen is on the paper. If alternatively they start to draw without having obtained an adequate overview, the reaction time will not be prolonged, but the movements will be slower because of longer movement times on the paper or longer hesitations above the paper and longer reinspections. There will also be more errors in the resulting drawing. The strategy chosen will probably be influenced by factors such as the instructions, the degree of complexity of the figure and the severity of depression. In this study the investigator gave strict instructions: he urged the participants to accomplish the tasks as quickly and as accurately as possible and to reinspect the figures only as an "emergency" measure, if no other solution was available. Also there were fewer stimuli (12 instead of 24) and the figures were less difficult. Furthermore the patient group that participated in this study was less depressed than those involved in previous studies. These factors can help to explain why the reaction times were prolonged: the patients put in more effort than the subjects in the past to inspect, memorize and plan the execution of the whole figure. These findings are in agreement with earlier theories about the role of motivation and sustained effort in controlled information processing (Cohen et al., 1982; Roy-Byrne et al. , 1986; Hart & Kwentus, 1987; Widlöcher & Hardy-Bayle, 1989; Tancer et al., 1990). In our third question, we manipulated the motor and cognitive demands of the task and detected changes in fine motor behaviour. The lines in the simple task (Task I) could be considered from a cognitive or from a motor point of view. Earlier results (Hulstijn et al., 1994) have suggested that only the lines that were more complex cognitively, i.e., the diagonal lines could differentiate between patient and control groups: the patients had longer reaction times before starting to draw these lines. The actual results are analogous, but the levels of significance were only borderline. Augmenting the complexity of the figures in Task I affected the reaction time and the movement time of the depressed patients more than the controls, as was shown by the significant interactions between

group and complexity. When drawing complex figures (Task II), complexity and unfamiliarity affected the movement time and specifically the pen-down time, the pen-up time and the pause time. It seems that increasing the complexity had a more disturbing influence on the movement itself, i.e., the movement time, the movement time pen down and the video reinspection time than on the reaction time. These disturbances of the movements themselves may be related to the planning and programming processes of the next strokes, but a motor execution component may also be involved.

It can be concluded that the fine motor activities of the majority of patients with a Major Depressive Episode, reflected in drawing tasks, were significantly retarded compared to the normal controls. Further analysis showed that retardation was already present in the very simple task of drawing a small straight line, as both reaction and movement were affected. Specific movement alterations could be isolated and it was possible to determine which strategies the patients had chosen. These results demonstrate further evidence of the cognitive and motor burden in major depression; further research should establish the link between the cognitive and motor burden on the one hand and underlying dopaminergic and subcortical dysfunction on the other. Recording and analysing figure drawing might be a valuable addition to the methods already in use to study psychomotor retardation.

Author Note

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CHANGES IN FINE MOTOR RETARDATION IN DEPRESSED PATIENTS TREATED WITH FLUOXETINE

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Abstract

Changes in psychomotor slowing were studied in 21 inpatients with a Major Depressive Episode. Fine motor retardation was measured and analysed using computer-aided drawing and figure-copying tasks at T0 (the start of 6-weeks treatment with fluoxetine 20 mg/day) and 5 weeks later (T1). The differences in reaction time between the patients and a group of healthy, matched controls at T0 had disappeared at T1. The initial motor deficit, expressed in longer movement times, had not improved at T1. These findings combined with the effect of manipulation of cognitive and motor demands, suggested that only cognitive processes had accelerated.

Key words: Psychomotor retardation; Depression; Figure drawing, Movement analysis; Antidepressant Treatment; Fluoxetine

Throughout the past decades psychomotor retardation has consistently been reported as a predictor of antidepressant response (Joyce and Paykel, 1989). However relevant research data are scarce, mainly because of the lack of reliable methods to quantify psychomotor retardation. In follow-up studies that used a clinical rating scale, such as the Salpêtrière Retardation Rating Scale, correlations were found between the severity of the retardation before treatment and the differences in the scores on the Hamilton Depression Rating Scale at the start of treatment and 4 weeks later (Widlöcher, 1983a). It was noticed in actometrical studies that the activity level progressively increased during treatment, while the duration of immobility decreased during clinical improvement (Royant-Parola et al., 1986). In studies that used choice reaction time tasks, both a motor and a cognitive component seemed to contribute to psychomotor slowing in the depressed patient. The decision time or the matching time decreased significantly during clinical improvement, which suggested cognitive improvement, while "pure" motor retardation remained unchanged (Ghozlan and Widlöcher, 1989; Rogers et al., 1987).

New technologies allow the more specific and detailed analysis of aspects of retardation and the way they change during treatment. The first reports stem from speech research. Earlier studies (Greden and Carroll, 1980; Greden et al., 1981; Hoffmann et al., 1985) had reported that antidepressant chemotherapy shortened the speech pause time during clinical improvement. Recently Kuny and Stassen (1993), using advanced techniques, found that several prominent features of speaking behaviour and voice characteristics were closely related to the time course of recovery from depression.

In our previous studies we measured and analysed fine motor retardation in depressed patients at the start of treatment and compared the results to those of normal control persons (Van Hoof et al., 1993; Van Mier and Hulstijn, 1993; Sabbe et al., 1996). It was concluded that compared to the normal control subjects, the writing and drawing behaviours of the large majority of depressed patients were slowed, although great inter-

individual differences were present. This manifested itself when they drew lines and simple and complex figures. Both the reaction time and movement time were prolonged, which suggested that fine motor retardation was the result of slowing of cognitive and motor processes.

In this study, following the preliminary research of Van Hoof et al. (1993), we examined the changes in depressive retardation at the start of treatment with antidepressive medication and at the end of the course five weeks later, in order to answer the following questions:

1. Does fine motor slowing in the patient group diminish or disappear after treatment?
2. If slowing improves after treatment, is it the cognitive and/or the motor slowing that improves?

Method

Subjects

Forty-two subjects participated in the study: twenty-one patients with a Major Depressive Episode (MDE) and twenty-one normal control subjects. In the study period all the MDE patients had been hospitalized at the Clinic of Psychiatry of the University Hospital Nijmegen, the Netherlands. All the patients aged between 18 and 65 years with an MDE and a minimum score of 18 on the Hamilton Depression Rating Scale (Hamilton, 1960), who were admitted between September 1992 and April 1994, were asked for informed consent after the nature of the study had been fully explained to them. Patients were excluded if they met one of the following criteria: motor disabilities affecting writing behaviour, severe cardiovascular or hepatic disease, renal failure and previous unsuccessful treatment with fluoxetine. The group comprised eleven male and ten female

patients. All the patients had a DSM III-R (American Psychiatric Association, 1987) diagnosis of a Major Depressive Episode, single episode (296.2) or recurrent (296.3); only 1 patient had a Bipolar Disorder, Depressed (296.5). The episode was severe in all the patients. Six patients did have psychotic features (code 4) and of the fifteen patients that remained, eleven met the criteria of major depression, melancholic type. Two patients had a subsidiary diagnosis of previous alcohol and benzodiazepine dependence. Three patients displayed a clinical state of agitation. For each patient there was a control subject, matched for age, sex and educational level.

Procedure and tasks

Once admitted to the study, all antidepressant drugs were stopped and any other psychotropic drugs were reduced as much as the condition of the patient allowed. Then fluoxetine 20 mg a day was administered to the MDE patients for six weeks. The tests were performed 1 week later (T0) and after 6 weeks (T1) of treatment. During this period, changes in the medication regimen were kept to a strict minimum. In fact, only very low doses of anxiolytics or neuroleptics, used by the patients with psychotic features (N=6), were allowed. For a discussion of the possible positive or negative effects of the use of this medication on the tasks used, see Sabbe et al., 1996.

Three clinical rating scales were scored at TO and T1: the Hamilton Depression Rating Scale (Hamilton, 1960), the Zung Self- Rating Scale (Zung, 1965) and the Salpêtrière Retardation Rating Scale (Widlöcher, 1983b). Tests consisted of a series of copying tasks with the aid of a pen on a graphics tablet. The movement registration method is discussed in the next paragraph. Stimuli differed in complexity and for task II also in familiarity (Figure 1). Complexity was defined as the number of strokes in a figure; familiarity could be perceptual or motor. For example letters are well-known perceptually and motorically, i.e., subjects are used to writing them, while figures, such as an arrow or a house, are well-known perceptually but not motorically; novel and nonsense patterns are unknown perceptually and motorically.

Three copying tasks were used:

- Task I analysed the degree of retardation in the drawing of lines and simple figures. The patients and controls had to copy 4 straight lines (one vertical, one horizontal and two diagonals) and 4 simple figures (Figure 1). All the stimuli were presented six times in random order. The lines could be divided on a cognitive level, i.e., in visuo-spatial processing and planning, in two classes: the vertical and horizontal lines were easier to draw than the two diagonal lines. In the simple figures the angle and circle were less complex than the diamond and spiral.
- The degree of complexity of the figures was increased in task II. Three types of stimulus had to be copied: combinations of capital letters, familiar figures and novel, nonsense patterns (Figure 1). Four stimuli of each type were presented with differing complexity, two with 4 strokes and two with 8 strokes.
- In task III a specific type of manipulation was executed that focussed on visuo-spatial processing. Eight figures, 4 combinations of letters and 4 figures (Figure 1) were presented, with the instruction to copy them at another angle, i.c. having rotated them through 90 degrees to the right.

Different sets of figures were presented at TO and T1 to avoid a learning effect in tasks II and III. Afterwards it appeared that although they were assigned at random, the figures presented in task II at T1 were more difficult than those presented in the corresponding task at T0.

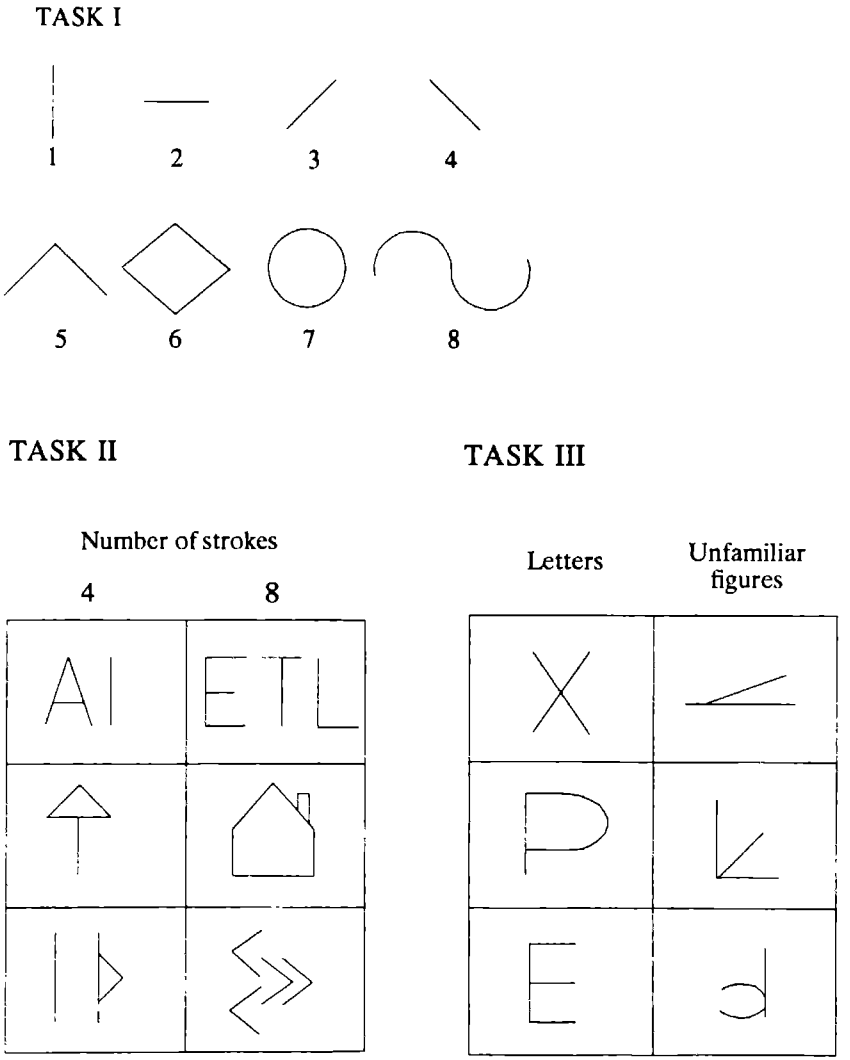


Figure 1. Stimulus designs used in Tasks I, II and III

In all the tasks, the participants received the standard instruction, as usual in this type of research, to draw as quickly and as accurately as possible. As soon as the pen touched the paper, the stimulus disappeared from the video viewing screen. In tasks II and III the subject could reinspect the figure by touching the pen against a red spot at the lower right hand corner of the digitiser. He/She was asked to do this only as an "emergency" measure, if he/she felt that otherwise too many errors would be made.

Prior to each task, a practice session was given in which the participants could become accustomed to the writing tablet and the procedure.

The investigators worked independently of the treatment staff. The three tasks were performed in a fixed order in 30 to 60 minutes. They all took place between two and five p.m., to avoid possible influences of circadian rhythm.

Recording and analysis

The drawing movements were recorded using a Calcomp 2300 digitiser, connected to a PC (63S386) that had been specially designed to measure pen pressure, with a precision of 2 g (Maarse et al., 1988).

The position of the pen on the graphics tablet and the axial pen force were recorded with a frequency of 100 Hz and a resolving power of 0.2 mm and 1 g, respectively. The following movement variables were measured: total time (TT), i.e., the sum of the reaction time and the movement time; reaction time (RT), i.e., the time interval between the presentation of the stimulus and the moment the pen touched the paper and the pressure threshold was exceeded; movement time (MT), i.e., the time interval between the first moment and last moment that the pressure threshold was exceeded. Movement time (MT) was divided into the time that the pen was on the paper and the pressure threshold was exceeded (movement time pen down: MTdown), the time that the pen was above the paper and the pressure was below the threshold (movement time pen up: MTup) and the video reinspection time (MTvideo), i.e., the length of time that the figure was reinspected.

The drawings in task II and task III were scored for errors by two independent investigators. Classification was made as follows:

- A-type error: the drawing more or less resembled the actual stimulus. Distinction was made between small and severe errors:

  -A1: rotation error of up to 30 degrees, distortion in proportions or in relations, segmentation of parts of the stimulus, fragmentation and alignment, omissions and additions (all up to 1/3 of the number of strokes of the original stimulus); also the drawings in which corrections had been made.

  -A2: rotation of more than 30 degrees; two-dimensionality instead of three-dimensionality; wrong letter(s); omissions, additions, reversal and distortion in form (all up to 2/3 of the number of strokes of the original stimulus).
- B-type error: the original stimulus could not be recognized because of too many omissions or additions, or no copy had been made.

Statistical analysis was performed with analyses of variance for each variable according to a repeated measurement design. The within-subject factors were complexity (Task I), complexity and familiarity (Task II) and familiarity (Task III), while the between-subject factor was group (patients versus controls).

Results

Clinical Rating Scales

The mean scores of the patient group on the three clinical rating scales at T0 and T1 were 24.7 (S.D.: 5.9) and 16.9 (S.D.: 9.2)($p=0.000$) for the Hamilton Depression Rating Scale, 62.9 (S.D.: 6.7) and 50.9 (S.D.: 14.8)($p=0.001$) for the Zung Self-Rating Scale and 26.O (S.D.: 5.6) and 18.6 (S.D.: 11.9)($p=0.01$) for the Salpêtrière Retardation Rating Scale. On

this latter scale the means of the subscores for the motor items, the speech items and the cognitive items at T0 were 1.4, 1.3 and 1.8, respectively, while at T1 they were 1.0, 0.9 and 1.3, respectively.

Copying Tasks

The results are presented task by task. Within each task, both the questions are discussed separately. To answer the first question about whether the retardation detected in the patient group diminished or even disappeared after treatment, the differences in the kinematic variables between the patient group and the control group (group effect) and the differences between TO and T1 (session effect) are presented. Obviously, the interactions between the group effects and the session effects contain the central information to answer this question.

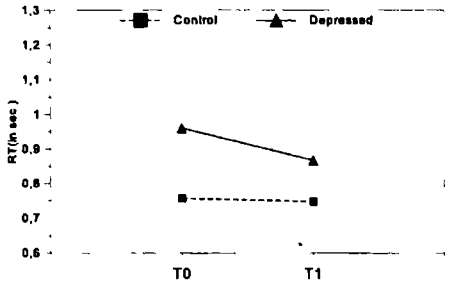
The second question about which component (cognitive or motor) improved if there was a positive treatment response, was investigated in two ways: by manipulating the complexity and familiarity within and between the subsequent tasks, and by making a detailed analysis of the different kinematic variables.

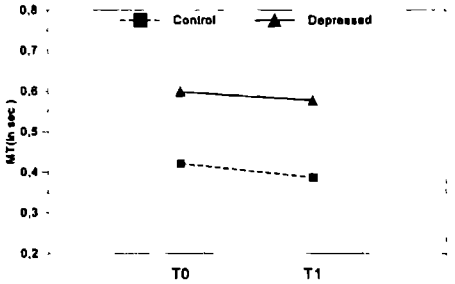
Task I: Lines and simple figures

The mean reaction and movement times at T0 and T1 are presented in Figure 2, the outcome of the analyses of variance in Table 1.

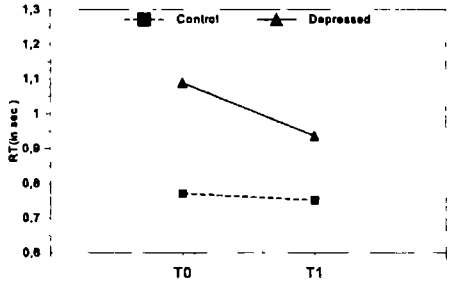
REACTION TIMES **MOVEMENT TIMES**

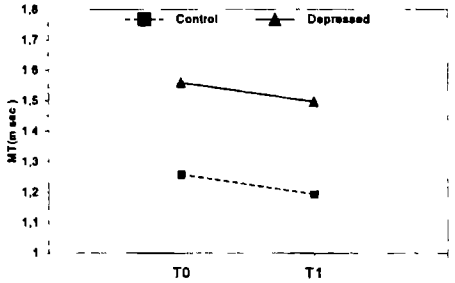
Task I: Lines



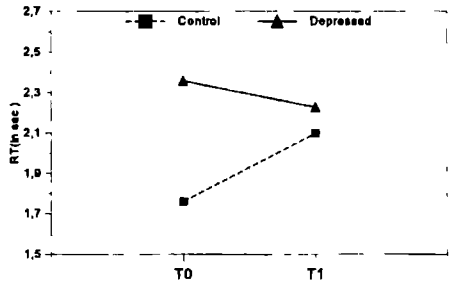


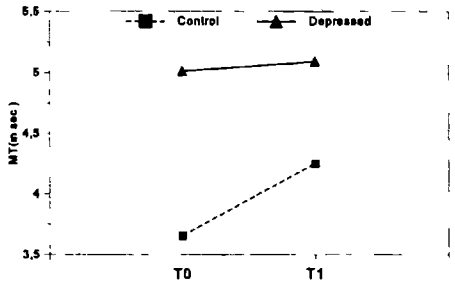
Task I : Simple Figures





Task II: Complex Figures





Task III: Rotation

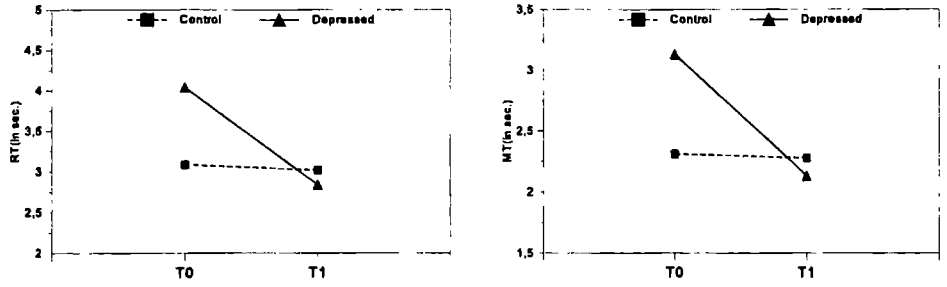


Figure 2. Mean reaction times (RT) and mean movement times (MT) of the depressed patients and the controls at T0 and T1 for copying lines and simple figures in Task I, complex figures in Task II and rotated figures in Task III.

*Lines

The reaction times in the patient group and the control group differed significantly and there was also a significant session effect. Figure 2 shows a reduction of the reaction time of the patient group after treatment, while no changes occurred in the control group. The group by session interaction was significant. It also appeared that the patients' decrease in reaction time between T0 and T1 was greater for the diagonal lines than for the vertical and horizontal lines (line type by session interaction within patient group: $F=6.65$, $p=0.01$). The mean movement time in the patient group at T0 was one and a half times longer than that in the control group, but did not decrease significantly after treatment.

*Simple Figures

The results for copying simple figures were similar to those for drawing lines (Figure 2). The group differences in reaction time were significant. The reduction in reaction time in the patient group after treatment did not occur in the control group. This was reflected in the significant group by session interaction. Additional analyses revealed that the decrease in reaction time was more apparent in the more complex figures (diamond-spiral) than in the simpler figures (angle-circle); the interactions between group and

complexity (F=5.87, p=0.020), and between group, complexity and session (F=6.92, p=0.012) were significant.

There was a significant group difference in movement time, but no significant decrease over session.

Task II: Complex Figures

The mean reaction and movement times at T0 and T1 are presented in Figure 2. In Figure 3 the effect of increasing complexity is shown: the mean reaction times at T0 and T1 for the letters, figures and patterns are presented separately. The changes in the different kinematic variables from T0 to T1 are shown in Figure 4. The outcome of the statistical tests can be found in Table 1.

Table 1
Results of the analyses of variance of tasks, I, II and III

	df	RT	MT	MTup	MTdown	MTvideo
Task I (lines)						
Group (G)	1	6 43 *	10 24 **			
Session (S)	1	4 94 *	1 04			
G × S	1	3 37 #	0 01			
Task I (simple figures)						
Group (G)	1	7 09 *	4 55 *			
Session (S)	1	7 09 *	205 36 ***			
G × S	1	4 31 *	0 01			
Task II (complex figures)						
Group (G)	1	2 11	4 52 *	0 13	3 69 #	5 93 *
Complexity (C)	1	87 32 ***	282 82 ***	246 23 ***	234 54 ***	33 02 ***
Session (S)	1	1 79	4 81 *	4 74 *	1 06	2 48
G × C	1	0 06	6 25 *	0 45	3 51 #	7 73 **
G × S	1	4 15 *	1 32	8 66 **	0 21	0 39
G × C × S	1	4 03 *	0 56	3 00 #	0 00	0 04
Task III (rotation)						
Group (G)	1	1 70	1 72	2 50	0 43	3 86 #
Session (S)	1	13 03 ***	8 67 **	13 07 ***	0 96	1 57
G × S	1	10 74 **	7 76 **	7 02 **	5 28 *	1 29

Note *F*-values for reaction time (RT), movement time (MT), movement time pen down (MTdown), movement time pen up (MTup) and video reinspection time (MTvideo)
# $P < 0.1$, * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$

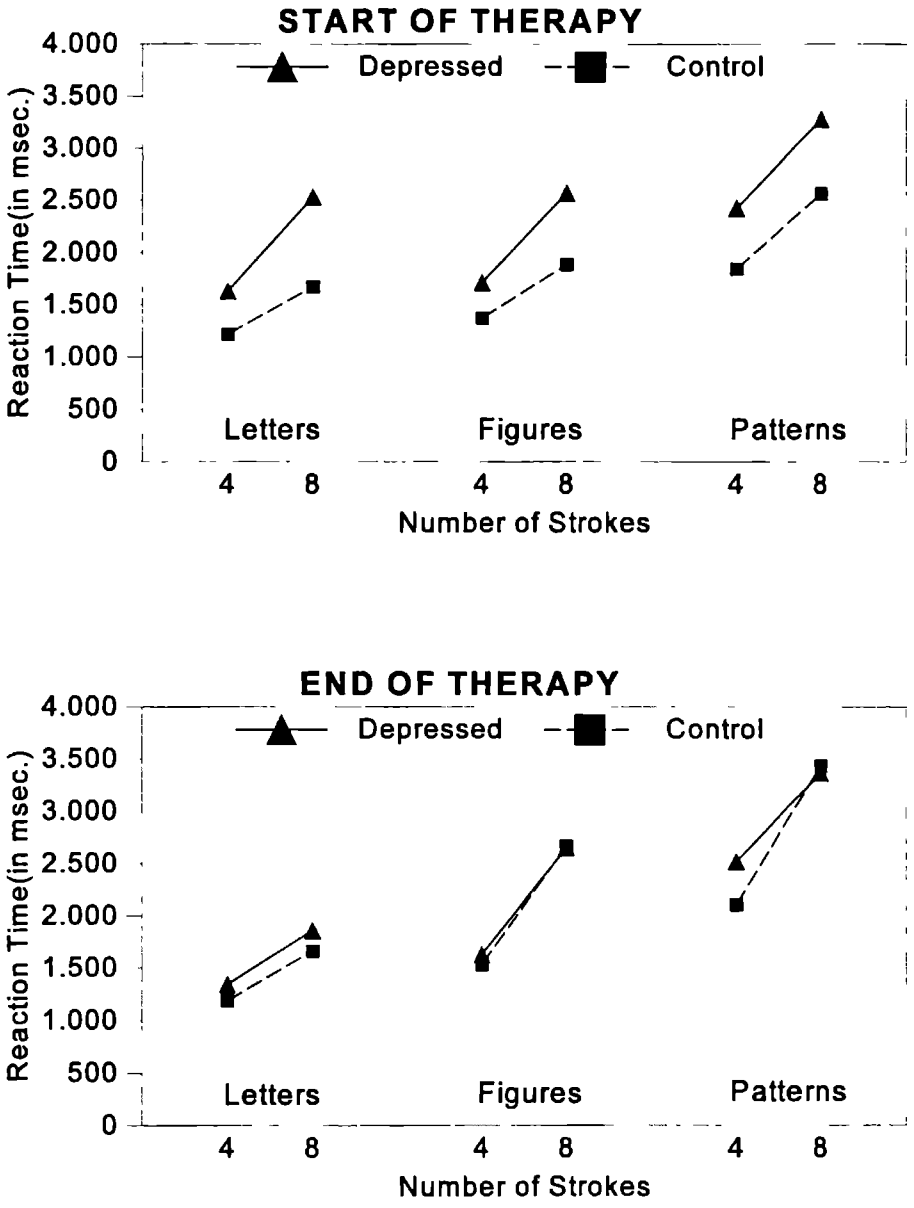


Figure 3. Mean reaction times (RT) of the depressed patients and the controls at T0 (top panel) and T1 (bottom panel) for copying complex figures in Task II

The reaction time in the control group at T1 was longer than at T0. In contrast with the simple figures that were the same at T1 and T0, the complex figures were dissimilar at T1 and T0. Post hoc, the figure set presented at T1 appeared to be more difficult than that presented at T0. Despite this, the reaction time in the patient group decreased slightly between T0 and T1. The significant interaction between group and session showed that the difference between patients and controls at T0 was significantly reduced at T1. The relative decrease in the reaction time in the patient group was more apparent for the more complex figures (8 lines versus 4 lines)(Figure 3). There was a significant interaction between group, complexity and session. Familiarity did not seem to be a relevant factor in this respect.

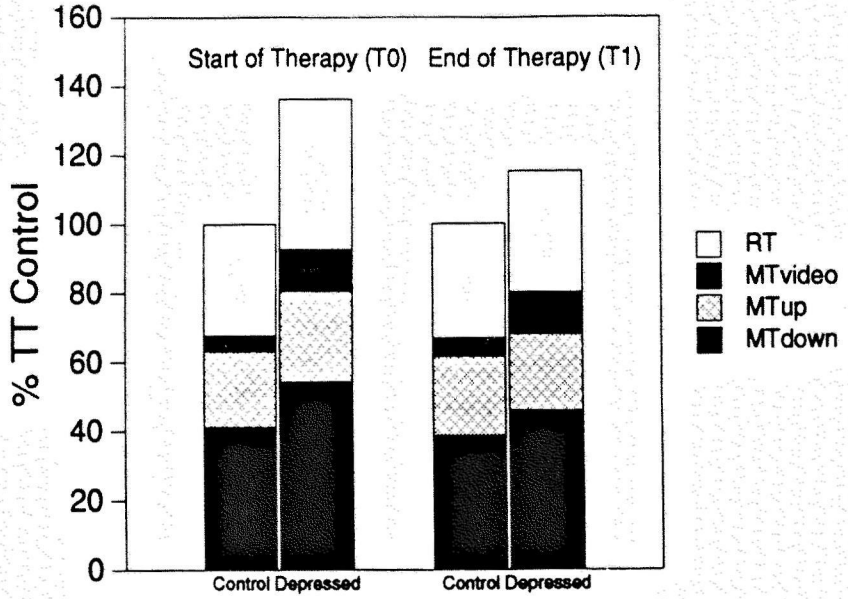


Figure 4. Mean total time (TT), mean reaction time (RT) and mean movement time (MT), divided into mean video reinspection time (MT video), mean movement time pen up (MTup) and mean movement time pen down (MTdown), of the depressed patients and the controls at T0 and T1 for copying complex figures in Task II. Because of a more difficult test set at T1 than at T0, all values are presented as percentages of the total time of the control group, scored as 100% at T0 and T1.

The movement time in the patient group was significantly longer than that in the control group. The difference between the groups was slightly reduced from T0 to T1. There was no significant interaction between group and session. However, when we considered the different components of the movement time in detail (Figure 4), there was a highly significant decrease of the movement time pen up (MTup) in the patient group.
There were no differences in the number or type of errors between the patient group and the control group at T0 or T1.

Task III: Rotation

The mean reaction and movement times at T0 and T1 are presented in Figure 2 and the results of the statistical tests in Table 1.
The reaction time in the patient group decreased significantly more than the reaction time in the control group from T0 to T1. At T1, the reaction time in the patient group was not significantly shorter than the reaction time in the control group. The overall (T0 and T1) group difference was not significant, while the interaction between group and session was clearly significant.
The pattern was similar for the movement time: the movement time in the patients decreased from T0 to T1, while that of the controls remained unchanged. The overall group difference was not significant. For the total movement time and for the movement time pen up (MTup) the interactions between group and session were highly significant. They also reached significance for the movement time pen down (MTdown).
There were no differences in the number or type of errors between the patient group and the control group at T0 or T1.

When we considered the group differences between the patient group and the control group at the start of treatment and at the end of the course five weeks later, the results were very univocal for nearly all drawing and copying tasks. There was a decrease in the reaction time in the patient group for copying lines, simple figures, complex figures and for drawing figures after rotation. In task III there was also a significant decrease in the movement time. Patients did not make significantly more or significantly fewer errors than the control subjects either at the start or at the end of treatment. Only differences in speed were found, not in accuracy.

If we take a decrease of the HDRS score of at least 40%, combined with a final maximum HDRS score of 18 as criteria for successful treatment, eleven patients had a successful outcome, while ten patients had not improved. The reaction times in the success group at T0 for tasks I (lines-simple figures) and II (complex figures) were significantly or nearly significantly longer than those in the failure group. For the simple figures, the RT in the success group was 1264 msec., while the RT in the failure group was 885 msec. From T0 to T1 there was a significant decrease in the reaction time in the success group (from 1264 to 1048 msec.). This was not the case in the failure group (from 855 to 788 msec.). The difference in the amount of decrease between the two groups (interaction between group and session) did not reach significance. When we considered the success group in detail, it appeared that five patients showed clear remission. They all had major depression with psychotic features. The other six improvers showed less clear improvement. They all had major depression, melancholic type. The improvement in the kinematic variables for these subgroups (improved psychotic patients, improved melancholic patients and non-improved patients) corresponded with clinical improvement. The decrease in reaction time and movement time in all tasks was largest in the psychotic depressive subgroup, moderate in the improved melancholic patients and absent in the non-improved patients. The interactions between subgroup and session did not reach significance, with the

exception of the MT and the MTup in the copying of the complex figures (Task II). These results underline the importance of psychomotor disturbance in psychotic and melancholic depression (Parker et al., 1993; Parker et al., 1994).

In answer to the second question regarding the nature of this reduction in fine motor retardation, the results clearly indicated an improvement in the so-called cognitive processes. This could be concluded from both strategies that were followed: analysis of the kinematic variables and manipulation of the cognitive and motor demands in the different tasks.

First, it was demonstrated in all tasks that the differences in reaction time between the patient group and the control group decreased significantly from T0 to T1 (significant interactions between group and session). The reaction time mainly reflects cognitive processing. In contrast, f.i. in tasks I and II there was no such a decrease in the differences in movement time, which indicates that the motor deficit itself, i.e., slowing of the motor processes, remained unchanged after six weeks of treatment. However, when we analysed this movement time in the complex figures in detail, it appeared that the movement time pen up decreased significantly between T0 and T1. This component mainly reflects the planning and programming processes, i.e., processes of a cognitive nature.

The other approach to the second question was to manipulate independent variables that are assumed to affect either cognitive or motor processes. In task I, it appeared that the reduction in reaction time between T0 and T1 was greater for the diagonal lines than for the vertical and horizontal lines. On a cognitive level, i.e., in visuo-spatial processing and planning, these diagonal lines are more difficult to draw than the orthogonal lines (Hulstijn et al., 1994). Complexity, which is considered to be a cognitive variable, was manipulated by augmenting the number of strokes in the figures in task I (simple figures) and task II (complex figures). In task II familiarity was changed by introducing figures that were perceptually well-known but motorically not practised, and totally unknown patterns. These stimuli were alternated with letters that were perceptually and motorically well-known. In both tasks, complexity clearly had more affected the reaction time in the patient group than the reaction time in the control group. The patients had greater

difficulty with accomplishing the more complex figures than the control group. After treatment, the patients had far less difficulty in task I and no difficulty in task II. In task III, there was a decrease in the reaction time, movement time, and the components the movement time pen up and the movement time pen down during treatment. We considered that this task was fundamentally different from the other tasks: it required a very complex visuo-spatial manoeuvre, that demanded greater cognitive effort. This caused slowing of all the components of the movement; during the movement time pen down, more "cognitive" readjustments (hand-eye coordination) probably also had to be made. Consequently, the results of this task have to be interpreted differently and they do not allow us to distinguish between the different processes involved.

It can be concluded from the analysis of the movement itself and manipulation of the different cognitive and motor variables that the reduction in psychomotor slowing after treatment was essentially the result of faster cognitive processing. The initial motor deficit remained unchanged and was responsible for the main difference that existed at the end of treatment between the patients and the controls. The changes in reaction time confirmed earlier results obtained with other methods of measuring psychomotor retardation. For example, elongation of the Speech Pause Time disappeared as the patients' condition improved after treatment with tricyclic antidepressants or electroconvulsive therapy (Greden et al., 1981). At present we have too little understanding of this reduction or disappearance of cognitive slowing and of the different psychological functions involved. It is also unclear whether the subsisting motor deficit is a state or trait marker and whether motor retardation changes during further treatment. Careful measurement and detailed analysis of fine motor behaviour during drawing and copying tasks will probably provide more precise answers to these questions and enhance the predictive validity of psychomotor variables in the antidepressant treatment response.

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RETARDATION IN DEPRESSION: ASSESSMENT OF THE MOTOR COMPONENT

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Submitted

Abstract

Psychomotor retardation in depression has mostly been assessed with tasks requiring both cognitive and motor processes. This study tested whether retardation could be measured if the cognitive demands of the task were minimal. One week after the start of antidepressant treatment, thirty inpatients with a Major Depressive Episode were compared to 30 healthy control persons, matched for age, sex and educational level. Tests consisted of ten simple drawing tasks that did not require any higher order cognitive processing. The kinematics of drawing movements were recorded using a specially designed pen, a digitising tablet and a PC. Patients showed marked motor slowing on all the tasks: longer movement durations, longer pauses and lower velocities. It could be concluded that psychomotor retardation in depressed patients treated with antidepressants has a strong motor component. These results open a new line of investigation into the motor aspects of depressive retardation, in contrast with the cognitive aspects.

Psychomotor retardation in depressed patients is considered to be the result of two types of slowing, cognitive and motor. The relative contribution of the slowing of cognitive and motor processes and their interrelationship still remain unclear. It is most likely that the cognitive and motor systems never function independently and that many phases of cognitive processing precede and maintain motor acts. However, it does not seem justified to conclude that motor slowing in depressed patients can be solely attributed to cognitive slowing. Using different methods to measure psychomotor retardation, there are indications for slowing of the motor processes themselves. This was suggested by direct clinical observation of psychomotor signs and symptoms (Parker et al., 1993; Parker and Hadzi-Pavlovic, 1996), by the scoring of retardation scales (e.g. the Salpêtrière Retardation Rating Scale, Widlöcher and Ghozlan, 1989), by simple motor tasks such as finger tapping and by the study of gross motor activity, i.e., actometry. However, by using these methods, it is not possible to discriminate precisely between the cognitive and motor components, or to manipulate them experimentally. Choice reaction time tasks showed both a prolonged decision time and movement time (Cornell and Suarez, 1984; Rogers et al., 1987). In speech research, mainly the speech pause time was prolonged, but not the phonation time (Greden and Carroll, 1981; Hoffmann et al., 1985; Kuny and Stassen, 1993).

A new computerised technique designed to measure and analyse writing and drawing movements enables more detailed study of cognitive and motor processing (Van Hoof et al., 1993; Van Mier and Hulstijn, 1993; Sabbe et al., 1996a). Earlier research into drawing movements using figure copying tasks has revealed major cognitive slowing in the depressed patients compared to normal controls, but has also suggested disturbance of the motor processes themselves (Sabbe et al., 1996a). This was manifested in longer movement times in the depressed patients than in the normal control persons in all the figure copying tasks, from the simplest to the most complex, and especially in prolongati-

on of the movement times "pen down". It was also found that the cognitive slowing disappeared almost totally after six weeks of treatment with fluoxetine 20 mg a day, whereas the motor slowing only decreased slightly (Sabbe et al., 1996b).

In this paper, we present the results of the first study which focused on slowing of the motor processes themselves. We analysed the kinematics of drawing movements during tasks that do not require any higher order cognitive processing and mainly rely on visuo-motor control.

Method

Subjects

Thirty patients, 17 females and 13 males, aged between 18 and 65 years with a Major Depressive Episode (DSM III-R) (American Psychiatric Association, 1987)(296.2 or 296.3) and a minimum score of 18 on the Hamilton Depression Rating Scale (Hamilton, 1960), were recruited from consecutive admissions to the Department of Psychiatry at the University Hospital Nijmegen, the Netherlands. The diagnosis was made after an extensive and detailed auto- and hetero-anamnestic interview. Two patients were excluded because they were suffering from motor disabilities that affected writing behaviour, and two other patients were excluded because of severe cardiovascular or hepatic disease.

The episode was severe in all the patients. Six patients had psychotic features. In two patients, the current episode was part of a bipolar disorder. Two patients had a subsidiary diagnosis of previous alcohol and benzodiazepine dependence. Three patients displayed a clinical state of agitation.

For each patient, a healthy normal control subject was selected, matched for age, sex and educational level.

After receiving a complete description of the study, written informed consent was obtained from all the subjects.

Procedure and tasks

Once admitted to the study, all antidepressant drugs were gradually stopped and other psychotropic drugs were slowly reduced as much as the condition of the patient allowed. Patients remained on low doses of benzodiazepines (N=14), neuroleptics (N=2) or a combination of the two (N=5). Twenty-four patients received fluoxetine 20 mg a day, while 3 patients received tricyclic antidepressants 75-125 mg a day. Tests were performed 1 week later and consisted of ten drawing tasks that had to be performed with the aid of a pen on a graphics tablet (Figure 1). The instruction was to draw as quickly and as accurately as possible. The ten trials were performed in a fixed order in about five minutes. The test took place between 2:00 and 5:00 p.m. to avoid any possible influences of the circadian rhythm and formed part of a larger test procedure (Sabbe et al., 1996a). At the same time the Hamilton Depression Rating Scale (Hamilton, 1960) and the Salpêtrière Retardation Rating Scale (Widlöcher and Ghozlan, 1989) were also administered.

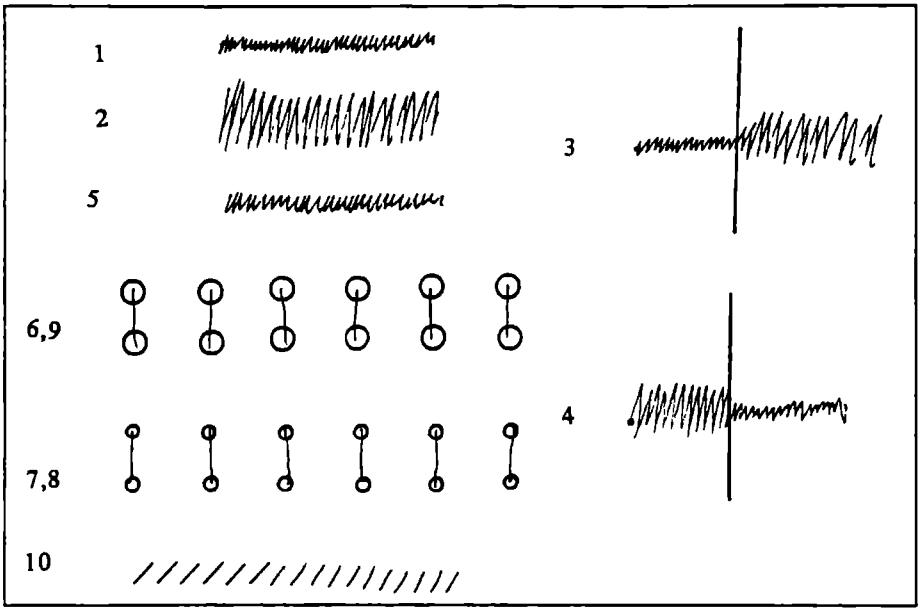

Figure 1 Stimulus designs used in trials 1-10 Example of a patient's drawing in trials 1-10

In trials 1 to 5, the subjects had to make a long series of connecting ascending and descending lines, with a small (3 to 4 mm) size (trial 1) or a large (± 10 mm) size (trial 2). They were also asked to change the size from 3 to 10 mm and from 10 to 3 mm in trials 3 and 4, respectively. By changing the size of the lines we wanted to investigate whether the depressed patients would increase their velocity during larger movements or if this was not the case, whether they would need longer movement times. In trial 5, the movement executed in trial 1 had to be repeated after the subjects were urged to complete the task as quickly as possible. This trial was designed to determine whether the patients were capable of increasing the velocity of the movement. The simple drawing tasks in trials 6 to 9 drew on more precise planning and programming processes than those in the previous tasks. They could be considered as a variant of Fitts' task: two vertically placed open circles had to be connected with a line of ± 10 mm from the centres of the circles. Per trial, 6 lines had to be drawn. The circle diameter was 0.5 cm in trials 6 and 9 (large

target) and O.25 cm (small target) in trials 7 and 8. In trial 10, the subjects had to continue the drawing of oblique lines of ± 10 mm until the line was complete. This enabled us to compare the results of the previous trials to those of a "freer" type of movement.

Recording and analysis

The drawing movements were recorded using a Calcomp 2300 digitiser connected to a PC and a pen that had been designed specially to measure pen pressure. The position of the pen on the graphics tablet and the axial pen force were recorded with a frequency of 100 Hz and a resolution of 0.2 mm and 1 g, respectively (Maarse et al., 1988). In all the trials, we measured the movement time (MT) per line and the mean absolute velocity per line. In trials 6-10, occasional pen-stops and pen-lifts were included in the MT, but excluded from the velocity calculations. In these trials, we also measured time intervals between lines (MTbetween).
Statistical analysis was performed using Manova with group as the between subject factor and length or target size as the within subject factor.

Results

Drawing tasks

There were no significant differences in the numbers of lines drawn (Figure 2); means of trials 1 to 5 were 31.5 (S.D. 7.7) for patients and 31.0 (S.D. 8.6) for controls.

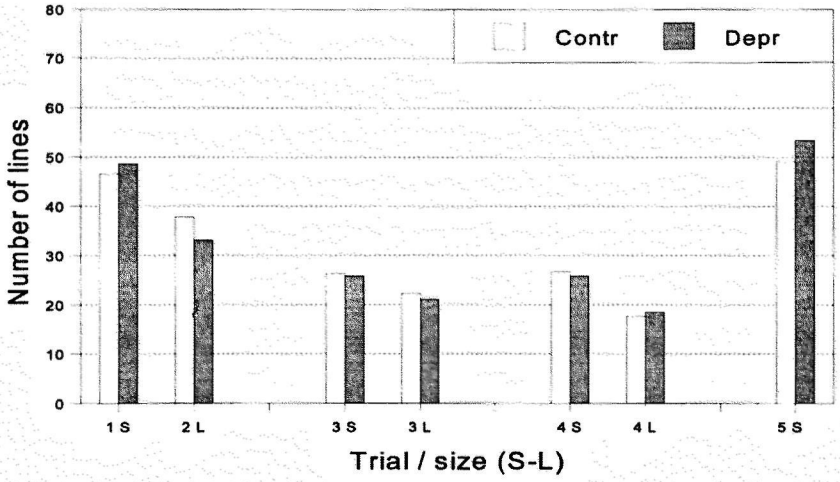

Figure 2. Mean number of lines drawn by the depressed patients and their controls in trials 1 to 5. S=small size (3 mm lines); L=large size (10 mm lines)

In all the trials, except for trial 10, the mean MT per line in the patient group was significantly longer than in the control group (Table 1) (Figure 3).

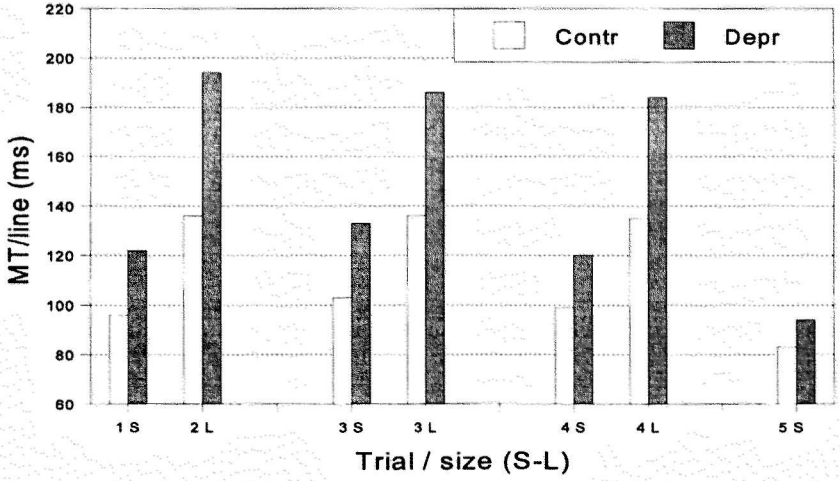

Figure 3. Mean movement time (MT) per line of the patient group and control group in trials 1 to 5. S=small size (3 mm lines); L=large size (10 mm lines)

Table 1 Mean Scores and Standard Deviations of the Kinematic Variables in All Trials for Depressed Patients (N=30) and Control Subjects (N=30)

	MT (msec)			MTbetween (msec)			Velocity (cm/sec)		
	P	C	F	P	C	F	P	C	F
df			(1, 58)			(1, 58)			(1, 58)
Trials 1-4 small (3 mm lines)									
mean	125	99	11 33**				2 83	3 76	11 73**
SD	38	17					1 08	1 03	
Trials 1-4 large (10 mm lines)									
mean	188	136	9 06**				6 26	8 79	9 88**
SD	89	34					3 09	3 14	
Trial 5									
mean	94	83	7 51**				4 24	5 26	2 69
SD	18	14					2 50	2 36	
Trials 6-9									
mean	799	444	16 21***	999	837	17 85***	2 11	4 05	31 80***
SD	415	245		150	148		0 81	1 70	
Trial 10									
mean	361	247	3 29	774	637	6 95*	2 68	3 48	7 60**
SD	319	133		223	175		1 04	1 19	

MT = Movement time, MTbetween = time interval between lines

F-values are given for group differences

* $p < 0\ 05$, ** $p < 0\ 01$, *** $p < 0\ 001$

In trials 6 to 10, the mean MT between was also significantly longer in the patient group. The mean distance per line in all the trials was the same in the patients and controls. In all the trials, the mean velocity per line in the patient group was far lower than that in the control group; the difference in mean velocity between the two groups was not significant in trial 5, which indicated that when speed was an important factor, the patient group was capable of increasing the velocity of movement. The differences in MT and velocity between the two groups tended to be larger when the lines were larger (trials 1 to 4) (group*size: for MT: F=3.41, df=1, 58, p=0.070 and for velocity F=6.32, df= 1, 58,

p=0.015) or when greater accuracy was required (trials 6 to 9) (group*size of target: for MT: F=4.97, df=1, 58, p=0.030 and for velocity: F=1.76, df=1, 58,p=0.190) (Figure 4).

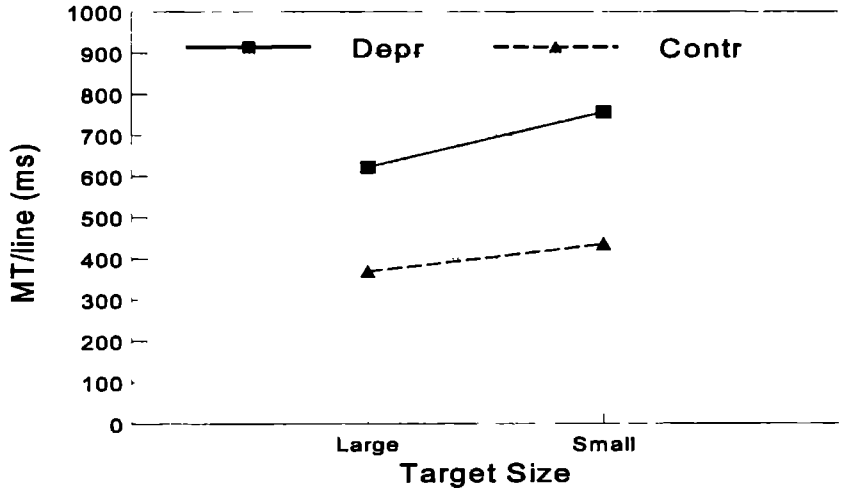

Figure 4 Mean movement time (MT) per line of the patient group and control group in trials 6 to 9. S=small target; L=large target

When studying trials 1 and 2 (Figure 5), it was found that the mean MT per line was longer in the first quarter of the movement than in the remaining quarters (group*special contrast: trial 1: F=6.02, df=1, 58, p=0.017 and trial 2: F=3.60, df=1, 58, p=0.063).

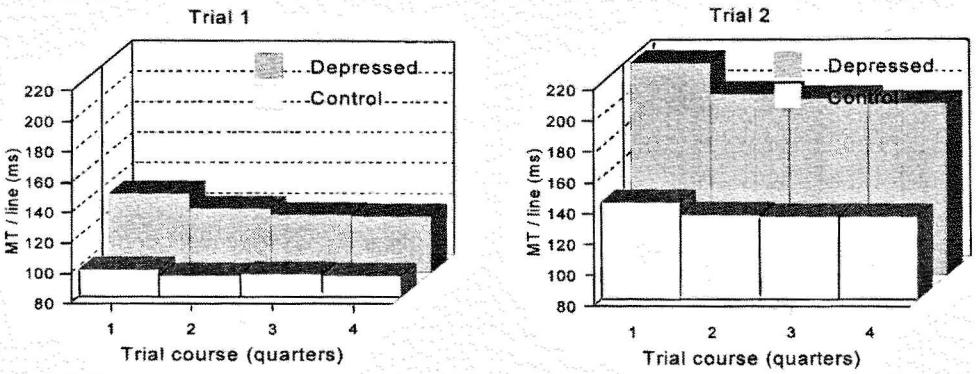

Figure 5. Mean movement time (MT) per line of the patient group and control group for each quarter of trials 1 (left panel) and 2 (right panel) separately

In trials 6 to 9, the mean MT was longer while drawing the first line (special contrast between line 1 and lines 2 to 5: F=6.86, df=1, 58, p=0.011) (Figure 6).

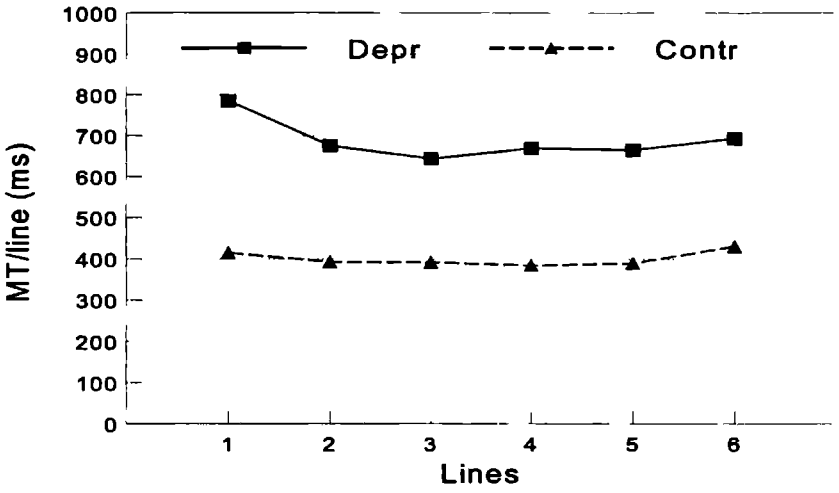

Figure 6 Mean movement time (MT) per line of the patient group and control group for each line of trials 6 to 9 separately

Clinical scales, medication and kinematic variables

The mean score and standard deviation in the patient group were 23.9 $\pm$ 5.8 on the Hamilton Depression Rating Scale, while they were 23.2 $\pm$ 7.0 on the Salpêtrière Retardation Rating Scale. No correlations were found between the use of co-medication and the kinematic variables. Only a few correlations appeared between the clinical scales and the kinematic variables.

The results indicated clearly that there was definite slowing of the visuo-motor control processes in the depressed inpatients who were receiving antidepressant treatment. They did not show a tendency to reduce the number or the size of lines. Motor slowing was also clearly apparent in the longer movement durations and lower velocities. These findings refine earlier results from studies that used simple motor tasks, actometry and choice reaction time tasks (Cornell and Suarez, 1984; Rogers et al., 1987), or analysed the outcome of speech research (Greden and Carroll, 1981; Hoffmann et al., 1985; Kuny and Stassen, 1993). They also reconfirmed the existence of more "pure" motor slowing, as was already detected in our previous work (Sabbe et al., 1996a), in which we used figure copying tasks that did not require higher order cognitive processing. In the latter tasks, the depressed patients not only displayed longer reaction times, but also longer movement times than the control persons; further analysis showed that this increase in movement time was partly due to longer movement times "pen down", (i.e., mainly to slowing of the motor processes themselves) but not to intermediate pauses, in which the next movements were planned. We concluded that depressive retardation, apparent in all tasks from the simplest to the most complex, had a double origin, cognitive and motor. The present study shows clearly that this motor component is present in very simple movements, such as rapid up and down movements and drawing lines.

It should be mentioned that our patient group was not medication-free. Almost all the patients were receiving antidepressant medication; more than half were receiving low doses of benzodiazepines and seven of them low doses of neuroleptic medication. It cannot be excluded that this medication had an influence on our results, although no correlations were found between the use of medication and the kinematic variables.

Detailed analysis of the drawing movements allowed the precise determination of the pattern and nature of this motor slowing. The slowing increased by increasing the size of the movement (trials 2 to 4) or by increasing the accuracy demands (trials 6 to 9). Motor

slowing appeared to be greater in the first quarter of the movement (trials 1 and 2) and while drawing the first lines (trials 6 to 9), than during the later course of the movement, which indicated initiation difficulties. The notion "initiation delay" means that the patients needed more time to reach an optimum rate of execution than the control persons. Enhancing the motivation of the patients to increase speed led to higher velocity, but prolongation of the movement duration persisted. All these findings indicate problems in the sensori-motor programming processes particularly in the starting phase of the execution of movement. This was manifested in serious limitations in the speed of execution and in the capacity to accelerate the action. The motor slowing, apparent from this study and the cognitive slowing, found in our earlier work (Sabbe et al., 1996a and 1996b), are in agreement with theories about a general slowing of all activities, e.g. by lack of activation, and about a close interrelationship of cognitive and motor processing (Widlöcher and Hardy-Bayle, 1989).

These results confirmed that the execution of drawing tasks not only enabled the precise measurement of reaction and movement times, but also the detailed analysis of the movements themselves. Further study of this fine motor slowing should be directed at disentangling medication effects and disease effects and at following the course of motor slowing during and after treatment. This will contribute to diagnosing psychomotor alterations in affective disorders (Parker and Hadzi-Pavlovic, 1996) and predicting therapeutic effects.

Author note

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DEPRESSIVE RETARDATION AND TREATMENT WITH FLUOXETINE: ASSESSMENT OF THE MOTOR COMPONENT

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Abstract

Changes in motor slowing between the start and end of treatment were studied in 22 inpatients with a Major Depressive Episode and 22 normal, healthy control persons. The degree and pattern of motor slowing were measured and analysed using computer-aided simple drawing tasks that did not require any higher order cognitive processing. The patients were treated with fluoxetine 20 mg/day for 6 weeks. Tests took place after 1 week (T0) and 6 weeks (T1). At T0 patients showed marked slowing, apparent in longer movement times and lower velocities than their controls. The differences between groups increased as the size of the movement increased or the accuracy demands increased. In all the trials, patients showed clear initiation difficulties. At T1 the motor slowing of the depressed patients had improved, but not disappeared. Significant differences remained between the two groups.

Interest in psychomotor retardation as an important or even core symptom of the depressive syndrome (Widlöcher & Ghozlan, 1989; Parker et al., 1993) and of its melancholic and psychotic subtypes (Parker et al., 1994) is steadily growing. This is partly due to consistent reports on the predictive value of psychomotor slowing regarding the therapeutic effects of treatment with antidepressive medication and electroconvulsive therapy (Joyce & Paykel, 1989; Browning et al., 1986).

In most research, slowing in the depressed patient appears to be the result of two types of slowing: cognitive slowing and motor slowing. These two components are present in clinical observation instruments such as the Salpêtrière Retardation Rating Scale (Widlöcher and Ghozlan, 1989) and the CORE system (Parker, 1993); they were also present in studies that used choice reaction time tasks and speech analysis. It remains unclear how cognitive and especially motor slowing are influenced by treatment. In choice reaction time tasks, the decision time or the matching time decreased significantly during clinical improvement, while the movement time remained unchanged (Rogers et al., 1987; Ghozlan and Widlöcher, 1987; Widlöcher and Ghozlan, 1989). In early speech research it was found that the elongation of the speech pause time was reduced after treatment (Greden and Carroll, 1980; Greden et al., 1981; Godfrey and Knight, 1984; Hardy et al., 1984; Hoffmann et al., 1985); the phonation time itself was no longer in depressed patients than in normal controls. Later, using advanced technology, the number of speech variables involved has increased strongly (Nilsonne, 1988; Stassen et al.,1991; Flint et al., 1993); several of them were found to be closely related to the course of recovery (Kuny and Stassen, 1993). However, it was not clear whether these changes reflected the acceleration of cognitive or motor processing, or both.

By measuring and analysing drawing behaviour during figure copying tasks, we demonstrated that the cognitive slowing of depressed patients at the start of treatment

with antidepressive medication disappeared almost completely after treatment (Van Hoof et al., 1993; Sabbe et al., 1996b).

The same methodology was used in very simple drawing tasks that do not require any higher order cognitive processing and mainly draw on motor control processes of sensori-motor programming, coordination, initiation and execution of the muscle commands and of feedback processing. The rationale of the tasks that we developed especially for this purpose is described in the method section of this article. This test enabled us to analyse the motor component in depressive retardation in a more precise and more specific way than ever before (Sabbe et al., 1996). It was concluded that there was clear slowing of these motor processes in depressed patients and that this slowing was influenced by changes in the amplitude of the movement and by increasing the accuracy demands. By motivating the patients to increase speed, the movement time decreased, but the patient group had still significantly lower velocities than the control group. The results also indicated initiation difficulties in the patients.

These results were obtained at the start of treatment. In this study they were analysed in more detail. The effects at the end of treatment with fluoxetine 20 mg a day for 6 weeks, were also evaluated. The first question was whether the motor slowing observed in the depressed patients at the start of treatment with fluoxetine, had diminished or disappeared at the end. If the motor slowing persisted after treatment, the second question was how did the pattern of motor retardation change during treatment? Again we looked at the effects of changes in amplitude and accuracy of the movement, and of enhancing the motivation of the subjects to increase speed. Also the initiation phase of the movement was studied more closely.

Subjects

Twenty-two patients with a Major Depressive Episode (MDE) and twenty-two normal control subjects participated in this study. The patient group comprised the same subjects as those who participated in a previous study (Sabbe et al., 1996b); only one male patient (and a matched control person) were added to the group. All of them had been hospitalized at the Clinic of Psychiatry of the University Hospital Nijmegen, the Netherlands. For each patient a normal, healthy control subject was found, matched for age, sex and educational level.

The patients were selected as follows: all the patients aged between 18 and 65 years with an MDE and a minimum score of 18 on the Hamilton Depression Rating Scale (Hamilton, 1960) were asked for informed consent after the nature of the study had been fully explained to them. Patients were excluded if they met one of the following criteria: motor disabilities that affected writing behaviour, severe cardiovascular or hepatic disease, renal failure and previous unsuccessful treatment with fluoxetine. The group comprised twelve male and ten female patients. All the patients had a DSM III-R diagnosis of a Major Depressive Episode, single episode (296.2) or recurrent (296.3) (American Psychiatric Association, 1987); only 1 patient had a Bipolar Disorder, Depressed (296.5). The episode was severe in all the patients. Six patients did have psychotic features (code 4); of the sixteen other patients, twelve met the criteria of major depression, melancholic type. Two patients had a subsidiary diagnosis of previous alcohol and benzodiazepine dependence. Three patients displayed a clinical state of agitation.

Once admitted to the study, all antidepressant drugs were stopped and any other psychotropic drugs were reduced as much as the condition of the patient allowed. Then fluoxetine 20 mg a day was administered to the MDE patients for six weeks. The tests were performed 1 week after the start of treatment (T0) and after 6 weeks (T1) of treatment. During this period, changes in the medication regimen were kept to a strict minimum. In fact, only low doses of anxiolytics (N=11), neuroleptics (N=2), or a combination of the two (N=5), were allowed.

Tests consisted of ten drawing tasks (Figure 1); the instruction was to draw as quickly and as accurately as possible. In trials 1 to 5, the subjects had to make a long series of connecting ascending and descending movements, with a low (3 to 4 mm) amplitude (trial 1) and a high ($\pm$ 10 mm) amplitude (trial 2). They were also asked to change the amplitude from 3 to 10 mm and from 10 to 3 mm in trials 3 and 4, respectively. The question behind changing of the amplitude of the lines, was whether the depressed patients would increase their velocity during larger movements or if this was not the case, whether they would need longer movement times. In trial 5, the movement executed in trial 1 had to be repeated after the subjects were urged to complete the task as quickly as possible. This trial was designed to determine whether the patients were capable of increasing the velocity of movement. The simple drawing tasks in trials 6 to 9 drew on more precise planning and programming processes than those in the previous trials. They could be considered as a variant of Fitts' task (Magill, 1993): two vertically placed open circles had to be connected with a line of $\pm$ 10 mm from the centres of the circles. Per trial, 6 lines had to be drawn. The circle diameter was 0.50 cm in trials 6 and 9 and 0.25 cm in trials 7 and 8, in which greater accuracy of movement was needed. In trial 10, the subjects had to continue the drawing of oblique lines of $\pm$ 10 mm until the line was complete. This enabled us to compare the results of the previous trials to those of a "freer" type of movement.

Prior to the actual test, a practice session was given in which the participants could become accustomed to the procedure. The ten trials were performed in a fixed order in about 5 minutes. They were part of a larger test procedure (Sabbe et al., 1996b). All tests took place between 2 and 5 p.m. to avoid possible influences of circadian rhythm.

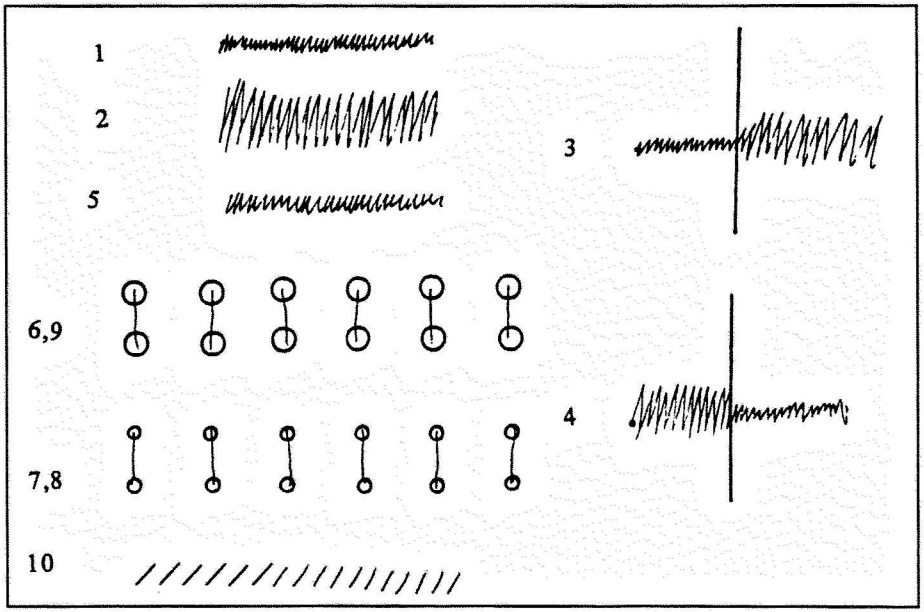

Figure 1. Stimulus designs used in trials 1 to 10

Recording and analysis

The drawing movements were recorded using a Calcomp 2300 digitiser, connected to a PC (63S386) that had been specially designed to measure pen pressure, with a precision of 2 g (Maarse, Janssen & Dexel, 1988). The position of the pen on the graphics tablet

and the axial pen force were recorded with a frequency of 100 Hz and a resolution of 0.2 mm and 1 g respectively.

In all the trials we measured the distance (Dist) and the movement time (MT) per line and the mean absolute velocity (Vel) per line. In trials 6 to 10 occasional pen-stops and pen-lifts (Pauses) were included in the MT, but excluded from the velocity calculations. In these trials we also measured the time intervals between drawing the lines, i.e., the time the pen was above the paper between lines (MTbetween).

Statistical analysis was performed using Manova with group as the between subject factor and length or target size as the within subject factor.

Results

Clinical Rating Scales

The mean scores of the patient group on the three clinical rating scales at T0 and T1 were 24.4 (S.D.: 5.9) and 16.9 (S.D.: 9.2) ($p=0.000$) on the Hamilton Depression Rating Scale, 59.2 (S.D.: 10.4) and 50.9 (S.D.: 14.8) ($p=0.001$) on the Zung Self Rating Scale and 24.5 (S.D.: 7.2) (Zung, 1965) and 18.2 (S.D.: 11.7) ($p=0.01$) for the Salpêtrière Retardation Rating Scale.

Drawing Tasks

Before describing the main results we make some general remarks about the presentation of the data. Because slowing is primarily defined as prolongation of the movement time, we first present the mean MT per line. However, if the distance is shorter, slowing can be better detected by analysing the velocity; therefore the Dist per line and the Vel per

line are also given. The means of the MT per line, the Dist per line and the Vel per line for trials 1 to 5 are presented in Figure 2. Of trials 3 and 4 the parts with low amplitude (L) were compared to the parts with high amplitude (H). The means of the MT per line, the Vel per line, the Pauses per line and the MTbetween per line for trials 6 to 9 are presented in Figure 3. The drawing movements between targets with a small size (S) were compared to the movements between targets with a large size (L). The results of trial 10 were compared to the scores of trials 6 to 9, but are not shown in the figures. The F- and p-values for all the trials are given in Table 1.

A general remark should also be made about the number of lines drawn by the patient group and the control group. It was not found that this number was lower for the depressed patients than for the control persons. In trials 1 to 5 there was no difference in the mean number of lines drawn between the two groups (mean patients at T0: 45.6, and at T1: 48.0; mean controls at T0: 43.8, and at T1: 49.9). In trial 10, the patients even drew more lines than the control persons (mean patients at T0: 17.0, and at T1: 18.3; mean controls at T0: 14.6, and at T1: 14.1; $F= 4.09$, $df= 1, 42$, $p=0.05$).

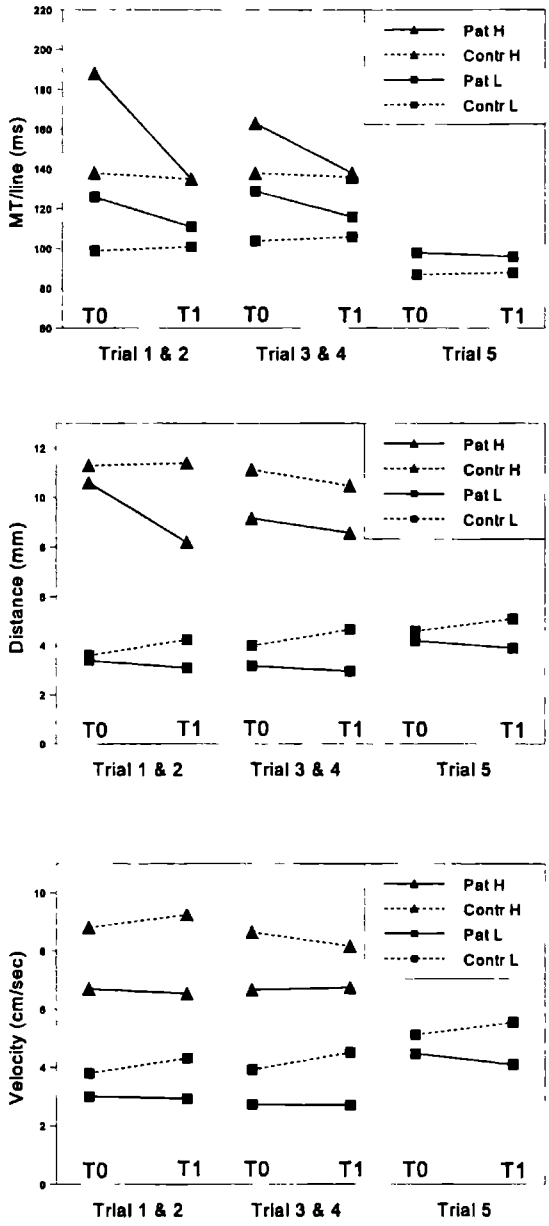

Figure 2. Mean movement times (MT) per line (upper panel), mean distances per line (middle panel) and mean velocities (Vel) per line (lower panel) of the depressed patients and the controls at the start (T0) and end (T1) of treatment for trials 1 & 2, 3 & 4 and 5.

L= low amplitude movements; H= high amplitude movements

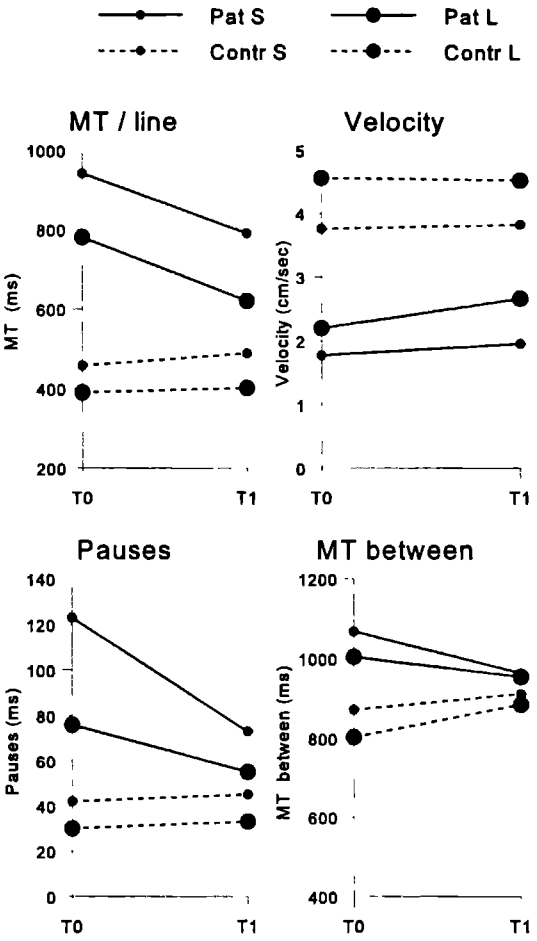

Figure 3. Mean movement times (MT) per line (upper left panel), mean velocities (Vel) per line (upper right panel), mean pauses (Pauses) per line (lower left panel) and mean movement times between lines (MTbetween) per line (lower right panel) of the depressed patients and the controls at the start (T0) and end (T1) of treatment for trials 6 & 9 and 7 & 8. S= small size targets; L= large size targets

Table 1 F-values for group differences - averaged on amplitude in trials 1 to 4, and on target size in trials 6 to 9 - on T0 and T1, and for Group by Session interactions

	T0	T1	Group by Session Interaction
	F	F	F
df	(1,42)	(1,42)	(1,42)
Trial 1 & 2 (low and high amplitude)			
MT / line	5 28 *	0 30	5 53 *
Distance	0 55	9 58 **	6 41 *
Velocity	5 04 *	9 06 **	1 90
Trial 3 & 4 (low and high amplitude within each trial)			
MT / line	3 44 #	0 36	3 61 #
Distance	5 12 *	8 53 **	0 96
Velocity	6 27 *	7 07 *	0 04
Trial 5 (low amplitude, as quick as possible)			
MT / line	4 86 *	2 34	5 21 *
Distance	0 54	4 35 *	4 36 *
Velocity	0 83	6 02 *	3 25 #
Trial 6 - 9 (connecting targets)			
MT / line	14 83 ***	12 07 ***	5 94 *
Velocity	26 88 ***	17 94 ***	1 11
Pauses	5 11 *	3 77 #	3 02 #
MT between	16 38 ***	0 39	2 43
Trial 10 (free lines)			
MT / line	2 47	0 02	3 00 #
Distance	4 86 *	3 01 #	1 02
Velocity	4 38 *	3 85 #	0 14
MT between	4 90 *	0 30	4 70 *

$p < 0\ 10$, * $p < 0\ 05$, ** $p \leq 0\ 01$, *** $p \leq 0\ 001$

Start of treatment.

At the start of treatment (T0) (Figures 2 and 3, lefthand values) the mean MT per line of the patient group was significantly or nearly significantly longer than that of the control group in all the trials. This was not because the lines were longer; on the contrary, in all the trials in which the size of the lines was not fixed ("free"), i.e., all the trials except for trials 6 to 9, the patient group drew shorter lines than the control group. Consequently, i.e., resulting from longer movement times by equal or shorter distances, in nearly all the trials the mean Vel per line at T0 was significantly lower in the patients than in the controls.

Question 1: Does motor slowing diminish or disappear during treatment?

This was analysed by comparing the results at T0 and T1, as is shown in Figures 2 and 3. It can be seen that the differences in mean MT per line between the two groups had decreased at T1, and even disappeared in some of the "free" trials: trial 2, high amplitude lines of trials 3 and 4, and trial 10. This reduction was reflected by a significant interaction between group and session for MT in trials 1 & 2, and 5; in trials 3 and 4 the same trend was present, but not significant ($p<0.10$). Also in the discrete lines of trials 6 to 9 (Figure 3, upper left panel) a similar reduction in the mean MT per line could be seen, but in contrast with trials 1 to 5 the mean MT per line of the patient group still remained 50% longer than that of the control group (Figure 3, upper left panel); the interaction between group and session was significant. In trials 6 to 9 the reduction of the mean MT per line was partly caused by a decrease in the number and duration of Pauses (Figure 3, lower left panel).

While in all the trials the mean MT per line decreased in the patient group between T0 and T1, the mean Vel per line (Figure 2, lower panel; Figure 3, upper right panel) was nearly the same at T0 and T1 and remained far lower at T1 than that of the control group.

Question 2: Does the pattern of motor slowing change during treatment?

The changes in the four following aspects of motor slowing are described: (1) the effects of increasing the amplitude of the movement (trials 1 to 4); (2) the effects of increasing the accuracy demands (trials 6 to 9); (3) the effects of urging the subject to increase the speed of execution to maximum (trials 1 and 5); (4) the initiation phase of the movement (trials 1, 2 and 6 to 9).

*Amplitude

Amplitude was manipulated in trials 1 to 4. Compare the upper lines (high amplitude) and lower lines (low amplitude) in Figure 2 (MT: upper panel; Vel: lower panel). At T0 greater amplitude resulted in increased, but not significant differences in mean MT per line and mean Vel per line between the two groups. At T1 these effects were less apparent or disappeared.

*Accuracy

Accuracy demands were manipulated in trials 6 to 9. Compare the lines between large targets and the lines between small targets in Figure 3. (MT: upper left panel; Vel: upper right panel). At T0 greater accuracy demands resulted in an increase in the differences in mean MT per line and mean Pauses per line between the two groups (group*size of target for MT per line: $F= 5.09$, $df= 1, 42$, $p= 0.029$ and for Pauses per line: $F= 4.66$, $df= 1, 42$, $p= 0.037$). For MT per line this effect of increasing the accuracy demands was the same at T1 (group*size of target for MT per line at T1: $F= 8.13$, $df= 1, 42$, $p= 0.007$) and for Pauses per line it disappeared ($F= .39$, $df= 1, 42$, $p= 0.536$).

*Speed

To evaluate the effect of urging the subject to execute the movement as fast as possible, the differences between trials 1 and 5 have to be considered (Figure 2). At T0 the difference in mean MT per line between the two groups was smaller in trial 5 than in trial 1; however, the difference between the two groups at T0 was still significant in trial 5. The difference in mean Vel per line at T0 was about the same in trials 1 and 5. When this

pattern at T0 - i.e., smaller, but still significant differences in the mean MT per line between the two groups in trial 5 than in trial 1 - was compared to the pattern at T1, it was found that the pattern was generally the same at both times.

*Initiation

When studying trials 1 and 2, it was found that at T0 the mean MT per line was longer in the first quarter of the movement than in the remaining quarters (group*course: trial 1: F= 3.10, df= 3, 126, p= 0.029 and trial 2: F= 2.30, df= 3, 126, p= 0.080) (for trial 1 see Figure 4 - left panel). In trials 6 to 9 the mean MT per line at T0 was longer for the first line (within group contrast between line 1 and lines 2 to 5: F=3.39, df=1, 42, p=0.073) (Figure 5 - left panel). At T1 these effects had disappeared: the interactions between group and quarter for MT in trials 1 and 2 were not significant (group*course: trial 1: F= 1.15, df=3, 126, p= 0.334 and trial 2: F= 1.06, df= 3, 126, p= 0.367) (for trial 1 see Figure 4 - right panel); the special contrast in trials 6 to 9 was not significant either (within group contrast between line 1 and lines 2 to 5: F= 0.00, df= 1, 42, p= 0.963) (Figure 5 - right panel).

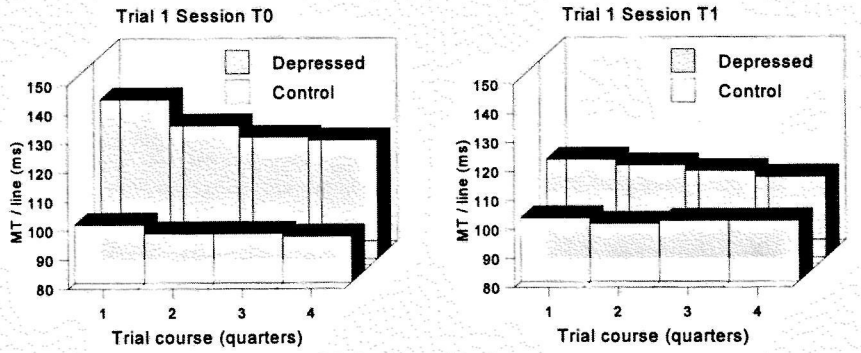

Figure 4. Mean movement times (MT) per line of the depressed patients and the controls at the start (T0) (left panel) and end (T1) (right panel) of treatment for each quarter of trial 1 separately

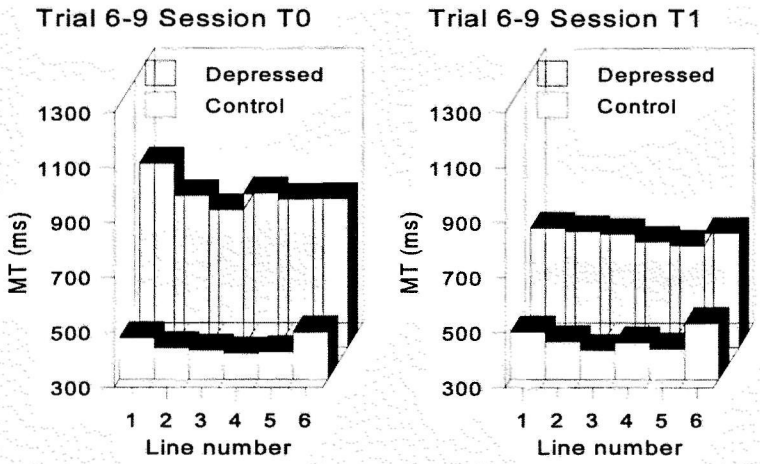

Figure 5. Mean movement times (MT) per line of the depressed patients and the controls at the start (T0) (left panel) and end (T1) (right panel) of treatment for each line of trials 6 to 9 separately

Discussion

In this study we compared the degree and the pattern of motor slowing between a group of inpatients with a Major Depressive Episode and of a group of normal, healthy control persons, matched for age, sex and educational level, at the start and end of treatment. The patients were treated with fluoxetine 20 mg a day for 6 weeks. Only small doses of other classes of psychotropic medication were allowed if absolutely necessary, and doses were kept stable during treatment. To measure fine motor slowing we used the same methodology as in previous studies (Van Hoof et al., 1993;

Van Mier and Hulstijn, 1993; Sabbe et al., 1996a; Sabbe et al., 1996b) and we designed very simple drawing tasks that mainly draw on motor control processes of sensorimotor programming, coordination, initiation and execution of the muscle commands and of feedback processing; these tasks do not require any higher order cognitive processing.

Slowing of the motor processes in the depressed patients at the start of treatment was clearly apparent from the significantly longer mean movement times per line and the significantly lower mean velocities per line of the patient group compared to the control group (Sabbe et al., 1996).

To answer the first question, the results clearly indicated that the slowing of motor processes in the depressed patients at the start of treatment (Sabbe et al., 1996) had diminished in nearly all the trials at the end of treatment, but nevertheless large differences remained between the patient and the control groups at the end. This reduction in motor slowing manifested itself as a decrease in the movement times in the patient group and not as an increase in the velocities. The movement times of the patient group decreased between the start and end of treatment, because the number and length of the pauses and stops during a movement were reduced and because the amplitude of the movement tended to be shorter. In the trials in which the size of the lines was not fixed, the patients were already drawing shorter lines than the control subjects at the start of treatment and even tended to reduce the distance after treatment. This tendency towards "micrographia" can be considered as a compensatory mechanism for motor slowing.

The reduction, but not disappearance of motor slowing in the depressed patients between the start and end of treatment is in contrast with the disappearance of cognitive slowing at the end of treatment that we found using figure copying tasks (Sabbe et al., 1996b). In that study we noted that the movement time pendown decreased between the start and end of treatment, but group by session interactions were not significant and large differences remained between the patient and control groups after treatment.

The findings of these studies enhance earlier conclusions drawn from research that used choice reaction time tasks, in which the movement times, if prolonged, did not change after recovery (Rogers et al., 1987; Ghozlan and Widlöcher, 1987; Ghozlan and Widlöcher, 1989).

It can be concluded that the patients could execute these very simple drawing movements faster at the end of treatment than at the start, but a large motor deficit persisted that was mainly reflected by lower velocities. This may have been due to the fact that only twelve out of the twenty-two patients could be considered as recovered, when a final score on the Hamilton Depression Rating Scale of a maximum of 18 and a decrease of a minimum of 40% on the same scale were used as success criteria. Ten patients did not improve. The success group could be divided in two subgroups: five patients, all of them with psychotic features, showed a clear remission; seven patients, which all met the criteria for a major depression, melancholic type, showed less clear improvement. When we compared these three subgroups: improved psychotic depressed patients, improved melancholic depressed patients and non-improved patients, clear, but not significant tendencies were found that the decrease in movement times between the start and end of treatment corresponded with clinical improvement. These results reconfirm the observations of Parker et al. of psychomotor disturbance in psychotic and melancholic depression (Parker et al., 1993; Parker et al., 1994). Finally it cannot be totally excluded that some tolerance to the medication (side-) effects could have played a role in the improvement in motor slowing between the start and end of treatment. However, we do not consider this to be an important factor as we have discussed earlier (Sabbe et al., 1996a).

In answer to the second question regarding the pattern of the fine motor slowing and its changes after treatment, it was found at the start of treatment that the differences in mean movement times and mean velocities between the patient and the control groups increased when the amplitude of the movement increased or the accuracy demands increased. The difference in mean movement time between the two groups decreased, but did not disappear when the subjects were urged to draw as fast as they could; thus

the patients were capable of speeding up, but nevertheless remained slower than their controls. In the "free" as well as in the "fixed" trials, the patient group displayed clear initiation difficulties. The latter result supports theories about pre-motor slowness, such as a delay in the initiation of movement (Widlöcher and Hardy-Bayle, 1989). When we evaluated the whole pattern at the end of treatment, the features were generally the same, but the differences between the groups were generally smaller, so that the various effects were smaller or had even disappeared; this was especially the case for the effect of increasing the amplitude and for the initiation difficulties.

It can be concluded that the slowing of motor processes in depressed inpatients decreased, but did not disappear after treatment. At the end of treatment, significant differences persisted between the patient group and the control group. The pattern of slowing was analogous at the start and end of treatment, but it was less marked at the end. The motor deficit that persisted at the end of treatment could be due to insufficient clinical remission. Further studies could perhaps show whether this motor deficit is still present in patients after total recovery, and if so, whether it disappears in the long-term or whether it has to be considered as a trait marker in depressed patients.

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Chapter 8

GENERAL DISCUSSION

1. Introduction

This Chapter presents a critical review of the studies described in this thesis: the findings are summarised and some concluding remarks are made. The aims of the studies are evaluated; the instruments, the selection of subjects, the procedure and the choice of tasks are discussed. An evaluation is made of the results of the studies in which depressed patients were compared to normal control persons at the start of treatment (Chapters 4 and 6) and between the start and end of treatment (Chapters 5 and 7). Also the validity and the reliability of the writing and drawing tasks are considered. Finally, the specificity of the findings is questioned and implications for future research are discussed.

2. Aims of the studies

This thesis evaluated how a new method to measure and analyse fine motor behaviour as manifest in writing and drawing movements contributes to the study of psychomotor retardation in depressed patients. Another aim was to investigate the cognitive and motor components of psychomotor retardation. In analyses using information processing models, no single stage or process was found to be specifically affected in depressive patients (Widlöcher and Hardy-Bayle, 1989). Therefore a central motivational deficit, operationalised as cognitive impairment and motor deficits in tasks which require sustained effort, has been put forward. This hypothesis has been supported in different types of study, using f.i. memory tasks or choice reaction time tasks (see Chapter 2). In memory research global dysfunction connected to the effortful nature of the task could be demonstrated (Widlöcher and Hardy-Bayle, 1989).However this explanation of psychomotor retardation in terms of lack of motivation, effort, arousal or drive has also been criticized. Widlöcher and Hardy-Bayle pointed out that motivation generally is conceptualised in terms of beliefs and judgments, whereas the slo-

wing in depression is of a far more fundamental nature than the level of semantic processing. These authors considered the psychomotor retardation in depressed patients to reflect global cognitive and motor slowing, which affected all information processing stages and was merely dependent on a deficit in activation and initiation of the actions. They hypothesized that this global and primary disorder does not affect the quality of performance, but rather the execution velocity. It could further be learned from the use of the Salpêtrière Retardation Rating Scale (SRRS) (Widlöcher and Ghozlan, 1989) that all items, motor-, cognitive- and language- related, co-vary; it was concluded that the relationship between motor slowing and cognitive slowing is even stricter than it is ordinarily assumed to be. Widlöcher and Hardy-Bayle also challenged the assumption that the depressed mood is translated into a decrease in motivation ("it doesn't matter what I do"). The degree of slowing will then correlate with the severity of the depression (Cohen et al., 1982; Günther et al., 1988). Widlöcher and Hardy-Bayle then asked, how can we explain that the performances of depressed patients are already altered in easy, "automatic" (in contrast with "controlled") tasks? They proposed inverting the relationship from "loss of motivation leads to slowness" to "slowness to activate is perceived as a loss of motivation".

This whole discussion prompted further investigation of the symptom of psychomotor retardation in depressed patients, especially exploration of cognitive and motor slowing, of their interrelationship and of the processes involved. Many questions arose: What is the nature of this slowing? Is it a decrease in velocity of execution of the movement as suggested by Widlöcher and Hardy-Bayle? Is the correlation between cognitive and motor aspects found with the SRRS also present in the fine motor behaviour of depressed patients? Is this slowing correlated with the severity of depression? Is it possible to investigate the role of motivation and effort and to look more carefully at the initiation phase of action? What are the effects of treatment? In the studies that are described in this thesis we evaluated whether with our new method, i.e., the measurement and analysis of the writing and drawing behaviour of the depressed patients, these questions could be answered in a much more detailed way.

3. Instruments

The technique and method introduced by Van Hoof et al. (1989) were used. They consisted of the registration of drawing and writing movements by means of a graphics tablet (digitiser), a specially designed electronic pen to measure pen pressure and a personal computer (see Appendix). In comparison with the traditional methods described in Chapter 2 of this thesis, this method of recording and analysing writing and drawing behaviour had several advantages. In contrast with (choice) reaction time tasks and the measurement of gross motor activity, by e.g. actometry, this new method enabled the much more precise analysis of the different components of the movement itself, the feedback processes used to adjust the movement and the (choice in) strategies to accomplish the whole task. Furthermore the careful selection of writing tasks allowed to some extent to analyse how cognitive and motor processes separately contributed to writing. Compared to speech research, this method has the advantage that it provides a limited number of variables, that can be overseen more easily and can be analysed and interpreted in terms of "slowness". The high degree of complexity of speech analysis and the large number of variables, made evaluation very difficult (Nilsonne, 1988; Stassen et al., 1991).

4. Subjects

Twenty inpatients, suffering from a Major Depressive Episode (MDE) (DSM III-R) and twenty normal healthy control persons, matched for age, sex and educational level, participated in the first studies (Chapter 3). An analogous group of twenty-two depressed patients and twenty-two control subjects participated in the studies described in Chapters 4 to 7. These samples were fairly small and a selection of the whole category of patients with MDE: they were all adult, severely depressed inpatients, hospitalized at a University Hospital. In this setting, all the patients aged between 18 and 65 years with

an MDE and a minimum score on the Hamilton Depression Rating Scale (Hamilton, 1960) of 18, who were consecutively admitted during a certain period, were asked to participate; only two patients refused and eight patients were excluded for various reasons (see Chapter 4).

It appeared that the large majority of the patients (17 out of 21 in the study described in Chapter 5 and 18 out of 22 in the study described in Chapter 7) were suffering from melancholic or psychotic depression. Our results therefore were obtained from patients that resemble those described recently by Parker et al. (Parker and Hadzi-Pavlovic, 1996). The patient group also comprised three patients who displayed clinical signs of agitation. Their results were no different from the other patients. This seems to be in agreement with the suggestion made by Parker and Hadzi-Pavlovic (1996; pp. 119-120) that patients with so-called retarded melancholia only show retardation, while those with agitated melancholia have a base of retardation upon which epochs of agitation are superimposed (a non-independent relationship).

5. Procedure and Tasks

In the studies described in Chapters 4 to 7, a double route of investigation was followed. Firstly, the psychomotor behaviour in a group of depressed patients was compared to the psychomotor behaviour in a group of control persons. Secondly, the psychomotor behaviour of the two groups was compared at the start of treatment with fluoxetine 20 mg per day and at the end, five weeks later. In the original design, the first test was planned to take place before the start of treatment, after a wash-out period of 8 days. However, it appeared to be practically impossible to stop all medication shortly after admission.

The test battery was set up in as broad a manner as possible to "catch" the greatest number of aspects of writing and drawing behaviour and in doing so, to minutely explore any deficits in depressed patients. Broadly speaking, the whole test can be considered

as a broad, standardized variety of tasks that cover a large field from fine motor activities on a 'simple level', i.e., not requiring any higher order cognitive processing, to tasks that do require complex visuo-spatial manoeuvres. The rationale of the choice of these specific tasks has been explained elsewhere (the Method sections of Chapters 3 to 7). In most trials, several concrete variants were worked out, in terms of the contents of the task (e.g. the nature and size of the movement, the length of the trial, the degree of cognitive and/or motor complexity) and the execution instruction; concerning the latter, in all the tasks except for trial 5 of the simple motor tasks (Chapters 6 and 7) equal emphasis was laid on the velocity and the accuracy of execution. Evaluation of these tasks indicated sufficient face validity; it showed that nearly all of them were capable of detecting aspects of psychomotor slowing in depressed patients. The exception was complex rotation task, which will not be used in future (Chapters 4 and 5) (see below).
It could be argued that too many tasks and variables were involved, so that statistical significance may have been achieved by chance. Therefore, in order to obtain a general overview, overall analyses were performed that confirmed the statistical significance of the differences between groups and between sessions (group by session interac-tions). These analyses confirmed the consistency of the findings (see below under 6).

6. Psychomotor slowing at the start of treatment

Three questions were addressed: (1) Are depressed patients slower to accomplish various drawing tasks than normal controls? (2) If so, on what aspects (dependent variables such as the reaction time and movement time and their components) does psychomotor retardation manifest itself most prominently? (3) When the more cognitive demands and the more motor demands - in as far as they can be separated - are manipulated independently, which manipulations had the most effect?
In relation with the first explorative question, it was found that the depressed patients as a group were slower than the control group while copying lines, simple figures, complex

figures and in the rotation task. These results were described in Chapter 4. It appeared that the patient group had longer reaction times (RT) and longer movement times (MT) than the control group in all the figure copying tasks. Prolongation of the RT mainly indicated slowing of the cognitive processes. Prolongation of the MT mainly indicated slowing of motor processes. When the copying tasks were more complex and the cognitive and motor demands were manipulated, it became clear that the movement time pen-down as well as the pauses and reinspections were prolonged in the patient group. Firstly, these findings confirmed the presence of both motor and cognitive slowing, as has already been demonstrated in many other studies that covered various fields of motor behaviour. Secondly, it was demonstrated that the patients followed a different strategy from that in earlier studies (Van Hoof et al., 1993 and Chapter 3; Van Mier and Hulstijn, 1993). In this study they took more time to view and memorise the whole figure, and to perhaps reinspect it, and consequently they made fewer errors than in the previous work. These findings indicate a major point: when confronted with their psychomotor deficit, the patients can follow different strategies to overcome their difficulties; by studying the results of individual patients, we found some indications that in severe depression other - more serial - strategies were used than in mild depression.

Some important remarks have to be made at this point. Firstly, when we considered the individual performance of each patient separately, great inter-individual differences were found. Most of the patients were moderately slow, some of them were two to five times slower than the controls, some were not retarded or were even faster than their controls. This has also been mentioned in earlier work with other measuring techniques, using choice reaction time paradigms (Ghozlan and Widlöcher, 1989) and speech analysis (Kuny and Stassen, 1993). One can speculate about the causes of this phenomenon. Maybe it indicates, as suggested by the work of Parker et al. and recently by Andreasen (XXth CINP congress, Melbourne, 1996) that MDE as a category is too broad and comprises too many different subgroups or subtypes of depressive disorders. Secondly, it has to be noted that all the patients were taking medication. By studying the

literature and by analysing the (lack of) correlations with the kinematic variables, it was concluded that the influence of medication whether positive or negative was probably minimal. However, it cannot be excluded that the results may have been different in a medication-free sample. Thirdly, slowing was present in all the copying tasks that were used: from the very simple lines to the complex rotation of unknown figures. The latter task appeared to be too difficult - slowing was so massive in all aspects of the task that the discriminatory capacity of the task was lost. This task will be omitted from future research, although visuo-spatial aspects remain important and should be included. Finally, a very intriguing finding was slowing of the more "pure" motor component, apparent in prolongation of the movement time pen-down in all tasks and in effects of increasing the motor demands.

The above was amply confirmed and the pattern of slowing could be observed in greater detail, in the later analysis of the motor tasks described in Chapter 6. From the study of these very simple drawing movements that did not require any higher order cognitive processing, it appeared that the patient group had longer movement times and lower velocities than the control group. This motor slowing increased when the amplitude of the movement or the accuracy demands increased, and was most apparent in the starting phase of the execution of the movement. Urging the patient to speed up to maximum led to an increase in the velocity, although the longer movement duration persisted.

The existence of slowing of the motor processes themselves remains a point of discussion in the literature. Slowing was found by most authors in (choice) RT tasks, while in speech research there were indications of disturbances in the processes involved in articulation itself. Motor slowing was also observed in studies that used finger tapping or automatic counting, and in actometrical studies. The existence of slowing of the motor processes, besides slowing of the cognitive processes, has now been clearly established in these simple drawing tasks. Although the two systems, cognitive and motor, cannot be separated clearly and probably never function independently and although many phases of cognitive processing precede and maintain motor acts, it is a major finding of these studies that the motor processes themselves were retarded in

these depressed patients. The nature of the motor slowing showed several important characteristics. Prolongation of the movement times was due to lower velocities. When compared to the normal control subjects, the patients did not show any tendency towards reducing the distance or the size of their movements, in contrast with "micrographia" as has been observed in patients using neuroleptic medication or suffering from Parkinson's disease (Hulstijn, 1996). The depressed patients showed a clear, but limited capacity to speed up, or to increase the velocity. Furthermore, they experienced difficulties reaching an optimum rate of execution of the movement. At present it is unknown whether these starting difficulties resemble those of patients with Parkinson's disease. In addition, when the distance that had to be drawn increased, slowing also increased; this was also the case when the accuracy demands were increased, which probably indicates difficulties with planning, programming or even motor execution processes. This whole pattern seems to be in agreement with Widlöcher's hypothesis of a deficit in the activation and initiation of actions, which results in decreased execution velocity. There are several possible explanations for this pattern of psychomotor slowing. Overall, it is not probable that mnemonic functions and motor control are impaired, in contrast with the more "conscious" planning, controlling and monitoring of both cognitive and motor processes. This can be due to general slowing of all activities, e.g. through a lack of activation, a slower biological clock and/or basic slowing of the rhythm of movement. It could also indicate slower "controlled" processing, slowing of all non-automatic processes that require great attentional effort, planning and monitoring. A third explanation concerns the intersection or junction of cognitive and motor processing in the programming and early starting phases of the motor act and stresses the close interrelationship between cognitive and motor processing.

In order to obtain an overall view on all the variables that were implicated at the start of treatment, further analyses were made of the results that were described in Chapters 4 and 5. The table that is listed below presents the results of the univariate F-tests (all with df 1, 41; one control subject had missing values on the simple motor tasks). As can be seen most variables showed a significant difference between depressive patients and

control subjects. Note the high F-values for the last two variables, presenting the results of the variant of Fitts' task ("joining the circles"). In a Manova stepdown analysis -in the order of the table- the first variable showed a significant group difference, and the last two variables ($p= 0.044$ for MT and $p= 0.001$ for MV). Since most of the variables were highly intercorrelated, these 16 tests are far from independent. The multivariate test on these 16 variables was highly significant (Pillais= .645. Approximate $F= 2.952$, df's were 16 and 26, $p= 0.007$).

To get an impression of the relation between these 16 variables factor analyses were run per subgroup and on the whole group. The results for each group were more or less similar, producing 3 or 4 factors (for control group and depressive group, respectively), of which the first two factors accounted for about 54 and 16 percent of the variance. The first factor might be called a reaction time-factor; after varimax rotation the RT values correlated 0.85, 0.91, 0.92 and 0.69 from simple motor tasks to the rotation task. The second factor might be called a velocity (MV)-factor (with the MV correlating 0.94, 0.93, 0.88 and 0.89 respectively). The MT-values of the copying tasks correlated equally strongly with both factors. The variables of the rapid up and down movements (motor trials 1-4) correlated most strongly with a separate third factor. The two variables of the motor trials 6-9 gave somewhat inconsistent results: they formed a separate factor for the depressed patients and correlated with the velocity-factor for the control subjects.

Table presenting the results of the univariate F-tests for the 16 variables of the tasks described in Chapter 4 (lines, simple figures, complex figures and rotation task) and in Chapter 5 (rapid up and down movements of trials 1-4 and the variant of Fitts' task in trials 6-9) RT= reaction time, MT all= total movement time, MV= mean velocity

	Variable	F	Sig of F
Lines	RT	7 78	008
	MT all	6 94	012
	MV	3 62	064
Simple figures	RT	8 48	006
	MT all	3 90	055
	MV	2 62	113
Complex figures	RT	4 37	043
	MT all	5 85	020
	MV	4 30	044
Rotation	RT	3 73	061
	MT all	4 61	038
	MV	2 97	092
Motor trials 1-4	MT all	4 23	046
	MV	5 31	026
Motor trials 6-9	MT all	14 30	000
	MV	26 16	000

7. Comparison between the start and the end of treatment

When the results of the depressed patients and the control persons were compared at the start (T0) and the end of treatment (T1) (Chapter 5), we found that in the patient group the slowing on the more cognitive aspects of the tasks had significantly decreased or disappeared at T1, while the slowing on the motor aspects had only diminished slightly at the end of treatment. The outcome of manipulating the cognitive and motor demands showed the same tendencies. Difficulties experienced by the patient group when complexity was increased diminished after therapy. After treatment, the responders were compared to the non-responders. It was noted that the responders showed greater slowing at the start of treatment than the non-responders (longer RT) and that slowing in the responders decreased significantly during treatment. From a diagnostic point of

view, the patient group could be divided into a subgroup of patients with psychotic depression who had clear remission, a subgroup of melancholic patients who improved significantly, but did not recover totally and a subgroup of non-improvers. The decreases in RT and MT were most clearly evident in the first subgroup, moderate in the second and absent in the third. These results are in line with the recent findings by Parker et al. that psychomotor disturbances are of particular relevance in psychotic and melancholic depressed patients and decrease after treatment with antidepressive medication and ECT (Parker et al., 1993; Hickie et al., 1990; Parker and Hadzi-Pavlovic, 1996). Overall we did not observe any change in the strategies that were followed at the start and end of therapy. At both points in time, the patients did not make more or fewer errors than the control persons. The medication and dosages that were being used were nearly the same at T0 and T1. It could be argued that the improvement of cognitive slowing was the result of greater tolerance to side-effects of the medication that was used, and that the persistence of motor slowing was the result of the use of the same medication at the same dosages at both measuring points. Possible influences of the medication cannot be excluded, although correlational analyses did not show any evidence of this; nor were there any indications for different effects on both components of psychomotor slowing.

The reduction in or disappearance of slowing on the cognitive aspects of the tasks during therapy has already been detected by means of other methods: in speech analysis, prolongation of the pause times disappeared after therapy with antidepressive medication or electroconvulsive therapy (Szabadi et al., 1976; Greden and Carroll, 1980; Greden et al., 1982; Hoffmann et al., 1985; Nilsonne, 1987; Kuny and Stassen, 1993) while in choice reaction time tasks, decision times were shorter after treatment (Cornell and Suarez, 1984; Rogers et al., 1987; Ghozlan and Widlöcher, 1987 and 1989). However it is unclear which process(es) undergo acceleration: perceptual, attentional, storage in the working memory, planning? General explanations such as an increase in energy, effort, motivation, arousal, do not sufficiently explain why cognitive slowing disappears, whereas motor slowing persists. Nor can changes in personality factors account for this.

In an attempt to interpret the lack of changes in motor slowing, the results of the second part of the test (that did not require any higher order cognitive processing) were analysed in great detail.

The analysis showed (Chapter 7) that in the patient group, the movement times at the end of therapy were significantly shorter than at the start, although large and significant differences remained between the patient group and the control group. There was no significant increase in velocity. The movement times in the patient group decreased between the start and end of treatment, because the number and length of the pauses and stops during the movement were reduced and because the amplitude of the movement tended to be shorter. The pattern of the motor slowing that was found at the end of therapy was generally the same as that observed at the start, but overall, the differences between the groups were smaller, so that the various effects had diminished or even disappeared; this was especially the case for the effect of increasing the amplitude and for the initiation difficulties.

The results of this analysis refine the conclusions drawn from earlier studies that used choice reaction time tasks, in which the movement times, if prolonged, did not change after recovery (Rogers et al., 1987; Ghozlan and Widlöcher, 1987 and 1989). The nature of this residual motor deficit after therapy has still not been elucidated: Could it be related to the fact that most of our patients did not recover totally from their depressed state? If so is it an indication that motor slowing is more closely related to the severity of the mood disturbance and/or to total recovery than cognitive slowing? Or is motor slowing a trait marker of these severely depressed patients that remains present even after the mood disturbance has diminished or disappeared? Or does motor slowing lie somewhere between these two extremes, e.g. as a symptom that will disappear totally after recovery from the depressive syndrome, but only after a relatively long period of time. In the latter case, "pure" motor slowing may form a symptom that is one of the last to ameliorate after the mood state has normalised; in this respect it is sometimes compared with sexual hypo- or alibidinaemia.

The difference in the course of cognitive and motor slowing between the start and end

of treatment, is a major finding in these studies. It demonstrates a clear difference between these two types of slowing in depressed patients and opposes theories that attribute motor slowing entirely to cognitive slowing, or that explain both types of slowing entirely in terms of (a lack of) effort, activation or motivation.

8. Validity and reliability

When reviewing the results of the different studies, it is important to discuss the validity and the reliability of the fine motor tasks that were used. On a descriptive level, it was found that in the figure copying tasks (Chapter 4) and the simple motor tasks (Chapter 6), the correlations between the scores on the Salpêtrière Retardation Rating Scale and the RT and MT were only weak or even absent. It is possible that these methods 'captured' slowing in different ways (see Discussion of Chapter 4). The content validity of figure copying and drawing tasks has been amply demonstrated (Thomassen and Van Galen, 1992; Hulstijn and Smits-Engelsman, 1995). Detailed analysis of the psychomotor behaviour of depressed patients during these tasks and of the changes between the start and end of treatment has enhanced and refined our insight into the cognitive and motor processes involved (see above and the Discussions of Chapters 4 to 7). Furthermore, there were indications of a certain predictive validity of the RT (and MT) at the start of treatment in the figure copying tasks (Chapters 3 and 5) and in the simple motor tasks (Chapter 7).

When evaluating the reliability of the tasks that were used, it has to be noted that in the treatment studies (Chapters 3, 5 and 7), the subjects were compared to themselves at T0 and T1 and that the results of retesting the control persons (five weeks after the first test) remained constant. For instance, the correlations between T0 and T1 for the control group were as follows: for the lines (Task I), simple figures (Task I) and complex figures (Task II) in Chapter 5: TT: .76, .75 and .89; RT: .76, .81 and .89; MT: .67, .72 and .85. For the complex figures in the rotation task (Task III) in Chapter 5

these correlations were weaker: TT: .60; RT: .38; MT: .53. For the simple motor trials 1-2, 3-4 and 6-9 in Chapter 7 these correlations were: MT: .76, .93 and .89; MV: .82, .88 and .86.

In all tasks, the standard deviations were large in the patient group and there was great inter-individual variability; this is analogous with the results obtained using other methods to measure psychomotor retardation (Chapter 2). In future research, further analysis of the sensitivity, the specificity and the test-retest reliability is needed, in order to further explore the predictive validity of the tasks that were used.

9. Specificity of the findings

In these explorative and descriptive studies on cognitive and motor slowing in a group of severely depressed inpatients, it can be asked how specific these findings are for depressed patients in general in comparison with patients suffering from other neurological and psychiatric disorders as Parkinson's disease, closed head injuries and schizophrenia. The first results of research into these categories of patients and into normal individuals using e.g. benzodiazepine medication, indicate a more specific pattern of slowing in depression than is generally assumed. In normal healthy persons who took a single dose of 15 mg diazepam, Scheres et al. (1996) found that only non-automated cognitive processes were disturbed. Van Mier and Hulstijn (1993) compared patients with closed head injuries, depressed patients and two groups of matched, normal controls. Both patient groups were slower than their controls (longer RT and MT); the pattern of slowing was different between the patient groups (far more errors in the depressive group than in the closed head injury group), and the compensation strategies, that were followed to overcome their difficulties were also different. In a recent study the Symbol Digit Substitution Test (that was also used in the third part of the test) was administered to a group of schizophrenic inpatients, a group of depressed inpatients and two groups of normal, matched controls. It appeared that the depressed

patients, besides longer decision or matching times, also demonstrated longer writing or movement times. Again this confirmed our findings of the existence of two components of slowing, cognitive and motor, in depressed patients. In contrast, the schizophrenic patients only showed longer matching times (Van Hoof et al., in prep.), indicating mainly difficulties in cognitive processing. Finally, in patients with Parkinson's disease it was found that movements were interrupted by many stops or pauses and that difficulties arose especially in the execution of sequential movements (for an overview, see Hulstijn, 1996).

10. Implications for future research

Future research should aim to provide more detailed and more accurate views on the specificity of cognitive and motor slowing in depressed patients. Also it should be directed at disentangling medication effects and disease effects and at providing more extensive information on the course of these two types of slowing in the long-term, i.e., in the 6 to 12 months after recovery. Long-term case studies would be useful, although first it will be necessary to investigate whether learning effects are associated with using these different tasks and if so, how they can be reduced. To analyse the long term course, comparisons could be made between groups of responders and non-responders to treatment. Also more insight is required into the underlying biological and structural mechanisms. Various approaches can be used to achieve this: studies on the effects of different types of medication whose working mechanisms are known; studies in which different methods are combined, such as alternative ways to measure psychomotor retardation (e.g. eye movements, gait and speech analysis), in combination with electrophysiological methods and neurochemical methods; and studies in which psychomotor behaviour is related to neuro-imaging. Several of these will be pursued in the near future.

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SUMMARY

The subject of this thesis is psychomotor retardation in depressed patients. In the daily clinical care of depressed patients, psychomotor changes are recognised by most practising psychiatrists as a clinically relevant symptom in the diagnosis and treatment of depression. In some theories they are considered to be the core symptom of depressive disorders, or of the melancholic and psychotic subgroups (Chapter 2).
However, an unambiguous definition of psychomotor alterations in depressed conditions is not yet available. Neither is there any clear insight into the different cognitive and/or motor processes involved. The aims of the studies described in this thesis were to evaluate how a new method to measure and analyse fine motor behaviour as manifest in writing and drawing movements, contributes to the study of psychomotor retardation and its cognitive and motor components in depressed patients.

In Chapter 2, the most used methods to measure psychomotor retardation in depressed patients are reviewed: rating and observation scales, the measurement and analysis of specific non-verbal behaviour, speech research, simple and choice reaction time measurements, the investigation of gross motor behaviour mostly by means of actometry, and of fine motor activities. Most studies using the various measuring techniques showed that, as a group, depressed patients were slower than normal, healthy control subjects. This retardation proved to be -either partially or entirely- of a cognitive nature. Whether motor retardation also occurs is less clear. In most studies in which the effects of treatment with antidepressants or electroconvulsive therapy were measured, a decrease in slowing was demonstrated after treatment.

In Chapter 3, the results of the first two studies are presented, conducted in each case on ten depressed inpatients. A new method to measure fine motor behaviour is described, namely the registration and analysis of writing and drawing behaviour by means of a graphics tablet (digitiser), a specially designed pen and a personal computer. This method is explained more extensively in the Appendix. Two types of figure copying task were administered: simple and complex. It was found that the patient groups, compared to

groups of matched, normal healthy control persons, had longer reaction times (RT) and longer movement times (MT) while copying the simple figures, but only longer MT, especially the movement times above the paper, while copying the complex figures. These findings indicated a clear cognitive component in the psychomotor retardation of the patients. The absence of any prolongation of the RT while copying the complex figures, combined with the findings that the patients made more errors and needed more and longer reinspections than the control subjects, suggested that a "serial" strategy was used by the patient group during the latter task. A small group of six patients was tested a second time after treatment. The changes in the scores on the Hamilton Depression Rating Scale (HDRS) between the two separate testing sessions correlated significantly with the changes in RT and MT while copying simple figures and with the changes in MT while copying complex figures. This indicated that repeating the measurement of drawing movements could be useful to evaluate changes in psychomotor slowing over time and possibly also the effects of treatment.

To confirm and extend these first results, a study was designed in which 22 depressed inpatients were tested after the start and after six weeks of treatment with fluoxetine 20 mg a day. A large variety of tasks were developed, in order to capture as many features of psychomotor slowing as possible. Besides very simple motor tasks that did not require any higher order cognitive processing, a complex rotation task was also introduced that involved a high degree of visuo-spatial difficulty. A full description of these tasks is presented in the Appendix.

Chapter 4 summarizes the results of the figure copying tasks obtained after the start of treatment. In general, the results of earlier studies were replicated. The patient group had a significantly longer RT and MT than the control group on all the tasks. Analysis of the RT, the MT and its components in the different tasks and the manipulation of the cognitive demands between and within the subsequent tasks, again clearly indicated cognitive slowing: a longer RT in the patients than in the controls on all the tasks, longer

pauses on the paper during the drawing movements and longer reinspections, significant interactions between group and complexity while copying simple figures. In addition, the results suggested a motor slowing component, which especially manifested itself in longer movement times "pen down". Large inter-individual differences in psychomotor slowing were found between the patients. There were no correlations between the results of the kinematic variables and the scales that measured the severity of depression while the correlations between the kinematic variables and the scores on the Salpêtrière Retardation Rating Scale were only weak. Although (co-) medication effects on the results of the drawing tasks could not be excluded, there were no arguments for positive or negative interference. The question of how this cognitive and motor slowing evolved between the start (TO) and end (T1) of therapy is addressed in Chapter 5.

It appeared that there was a significant decrease in RT between TO and T1 in the patient group. This was seen specifically in the patients with a good response to treatment (success group), i.e., the patients that showed a decrease in the score on the HDRS of a minimum of 40% and a final maximum HDRS score of 18, (n= eleven out of twenty-one patients, all with a Major Depressive Episode with psychotic features, or the melancholic subtype). Combined with a significant decrease in the movement time pen up between T0 and T1 and with a decrease in the difficulties that the patients experienced at the start of treatment while copying the more complex figures, these results indicated that the reduction in psychomotor slowing after treatment was essentially due to faster cognitive processing. The initial motor deficit remained unchanged and was responsible for the main difference that existed at the end of treatment between the patient group and the control group. The differences in cognitive and motor slowing between the start and the end of treatment formed the motivation to perform a detailed analysis of motor slowing itself. This was the subject of the study that is described in Chapter 6.

The ten trials that were used to explore the pattern of motor slowing are described in detail in the Appendix. The results of the 22 patients who participated in the previous

studies were added to those of 8 patients in the first study (Chapter 3). In these simple motor tasks that did not require any higher order cognitive processing, slowing was clearly apparent in the longer movement durations and lower velocities. Slowing increased when the amplitude of the movement or the accuracy demands increased. Motor slowing appeared to be greater in the first quarter of the rapid up and down drawing tasks and while drawing the first lines in Fitts' task than during the later course of the movement, which indicated "initiation" difficulties. Although urging the patients to increase speed led to higher velocity, prolongation of the movement duration persisted. This whole pattern may reflect problems in the sensori-motor programming processes, particularly in the starting phase of the execution of movement and is in agreement with theories about the general slowing of all activities in depression, e.g. through a lack of activation and about a close interrelationship between cognitive and motor processing.

In Chapter 7 the motor slowing explored at T0 was compared to the situation measured at T1. It was concluded that the slowing of motor processing at T0 had diminished in nearly all the trials at T1, but nevertheless large differences remained between the patient and the control groups at T1. This reduction in motor slowing manifested itself as a decrease in movement times, but not as an increase in velocity. Movement durations decreased because the number and length of the pauses and stops during the movement were reduced and because the amplitude of the movement tended to be shorter. At the end of treatment, the pattern of motor slowing was analogous with that at the start of treatment, as described in the previous Chapter. The features were generally the same, but the differences between the groups were smaller, so that the various effects were smaller or had even disappeared. A question that has not yet been resolved is whether this motor slowing, that diminished but did not disappear after treatment, was due to insufficient recovery or whether it should be interpreted as a state- or trait-related feature of the depressive condition.

The General Discussion of Chapter 8 presents a critical review of the studies described in this thesis. The aims are evaluated; the instruments, the selection of subjects, the procedure and the choice of tasks are discussed. An evaluation is made of the results, that were obtained. Also the validity and the reliability of the writing and drawing tasks are considered. Finally the specificity of the findings and implications for future research are discussed. Our results are compatible with the hypothesis of Widlöcher and Hardy-Bayle of a global dysfunction, dependent on a deficit in activation and initiation of the actions, connected to the effortful nature of the task, but already present in "automatic" behaviour. They are also in agreement with the conclusion that the retardation does not primarily affect the quality of the performance, but rather the execution velocity, although changes in strategy also can influence the performance. However, in contrast with their findings on an even stricter relationship between motor slowness and cognitive slowness than ordinarily assumed, our results show a different evolution of these components, when the start and the end of therapy are compared. It became clear (Chapter 7) that although reduced, an important motor deficit remained after treatment, whereas cognitive slowing had almost disappeared. The implications of this conclusion are discussed.

COMPTE RENDU

La présente thèse prend pour objet le ralentissement psychomoteur de patients dépressifs hospitalisés.

La plupart des psychiatres s'occupant des soins quotidiens de patients dépressifs, considèrent les changements psychomoteurs soit comme des symptômes soit comme un groupe de symptômes d'une grande pertinence clinique quant au diagnostic et au traitement de la dépression. Dans certaines théories, ces changements sont même considérés comme les symptômes centraux de la dépression majeure ou des dépressions des sous-types mélancolique et psychotique.

Cependant, on ne dispose pas d'une définition univoque des troubles psychomoteurs accompagnant la dépression. De même, une explication claire des aspects cognitifs et moteurs du ralentissement psychomoteur fait défaut. Or, la finalité des recherches rassemblées dans cette thèse est d'évaluer la contribution d'une nouvelle méthode à la description du ralentissement psychomoteur des patients dépressifs d'une part et de ses aspects cognitifs et moteurs d'autre part. La méthode en question consiste à mesurer et à analyser la fine motricité des mouvements d'écriture et de dessin.

Dans le Chapitre 2, nous fournissons un aperçu de la littérature scientifique consacrée au cours des quinze dernières années aux méthodes les plus fréquentes de mesurer le ralentissement psychomoteur de patients dépressifs: les échelles d'évaluation et d'observation; l'observation, la mesure et l'analyse du comportement spécifique non verbal; l'étude du langage; la mesure des temps de réaction simple et de choix; l'analyse de la grosse motricité - le plus souvent à l'aide de l'actométrie - et finalement de la fine motricité. La plupart des recherches démontrent que les groupes de patients dépressifs sont plus lents que les groupes de personnes de contrôle normales et en bonne santé. Ce ralentissement s'avère - partiellement ou complètement - de nature cognitive. L'existence d'un ralentissement moteur concomitant reste en ce moment un point de discussion. La grande majorité des études évaluant les effets de traitements à l'aide de médicaments antidépresseurs ou de la thérapie électroconvulsive, mentionnent une réduction du ralentissement après le traitement.

Le Chapitre 3 expose les résultats de nos deux premières études, effectuées chaque fois sur 10 patients dépressifs. Nous y expliquons la nouvelle méthode de mesurer le comportement moteur fin. Il s'agit nommément d'enregistrer et d'analyser des mouvements d'écriture et de dessin à l'aide d'une tablette d'écriture, d'une plume spécialement construite et d'un ordinateur. La méthode est plus amplement décrite dans l'Appendice. Nous avons utilisé des tâches de copiage de figures simples et de figures plus complexes. Il s'est avéré qu'en comparaison avec des groupes de personnes de contrôle normales et en bonne santé, les groupes de patients ont besoin de temps de réaction (RT) et de temps de mouvement (MT) plus longs en copiant les figures simples et de MT plus longs - surtout pour les mouvements au-dessus du papier - lors du copiage des figures complexes. L'absence de rallongement du RT en copiant les figures complexes, ainsi que le nombre plus élevé d'erreurs et de réinspections d'une durée également plus longue, indiquent une stratégie sérielle lors de l'exécution de la tâche expérimentale. Un groupe de six patients a été testé de nouveau après un traitement de médicaments antidépresseurs. Les changements mesurés à l'aide du Hamilton Depression Rating Scale (HDRS) entre les deux moments du test, étaient corrélatifs aux changements du RT et du MT pour les tâches de copiage de figures simples et avec les changements du MT pour le copiage de figures complexes. Ceci indique que l'observation répétée des mouvements de dessin pourrait servir à mesurer des changements psychomoteurs pendant un certain laps de temps, ou à mesurer les effets de traitements.

Afin de confirmer et d'approfondir ces premières données, nous avons conçu une étude où 22 patients hospitalisés pour dépression majeure sont testés au début et à la fin d'un traitement de six semaines à la fluoxétine à raison de 20 mg par jour. Nous avons élaboré une grande variété de tâches, dans le but d'examiner le plus grand nombre d'aspects du ralentissement psychomoteur. Outre des tâches motrices simples, où il n'est pas fait appel à des processus cognitifs d'ordre supérieur, nous avons également introduit une tâche de rotation très complexe d'un haut de degré de difficulté visuo-spatiale.

Le Chapitre 4 rassemble les résultats des tâches de copiage des figures. Généralement parlant, les résultats des premières études sont confirmés. Pour toutes les tâches, le groupe des patients montre des temps de réaction ainsi que des temps de mouvement significativement plus longs que le groupe de contrôle. Les analyses des temps de réaction, des temps de mouvement et de ses composantes ainsi que des manipulations cognitives entre et à l'intérieur des tâches successives, indiquent un ralentissement des processus cognitifs des patients: des RT plus longs chez les patients que chez les personnes de contrôle pour toutes les tâches, des hésitations plus prononcées au-dessus du papier pendant le mouvement d'écriture, ainsi que des réinspections plus longues. En plus, lors du copiage des figures simples, il s'est manifesté des interactions significatives entre groupe et complexité.

Finalement, les résultats démontrent un ralentissement moteur net. Celui-ci donne lieu à des temps de mouvement plus longs au moment où la plume se trouve sur le papier. Nous remarquons de grandes variations interindividuelles quant au degré de ce ralentissement psychomoteur. Il n'y a pas de corrélation entre les variables cinématiques et les échelles mesurant la gravité de la dépression; les corrélations entre ces variables cinématiques et les valeurs sur la Salpêtrière Retardation Rating Scale (SRRS) sont faibles. Bien que les effets de la (co-)médication sur les résultats des tâches d'écriture et de dessin ne puissent être exclus, il n'y a pas d'arguments en faveur de l'hypothèse d'une influence certaine de ces médicaments, ni dans le sens positif, ni dans le sens négatif. La question de savoir si et comment ce ralentissement cognitif et moteur évolue entre le début (T0) et la fin (T1) du traitement, est traitée dans le Chapitre 5.

Nous avons pu constater une réduction significative du RT entre T0 et T1. Cette observation vaut pour tous les patients, et surtout pour le sous-groupe des "répondeurs" au traitement, c'est-à-dire pour les patients dont la valeur au HDRS était réduite d'au moins 40% à la fin de traitement et ne dépassait pas 18. Il s'agit de 11 des 21 patients, tous souffrant d'une dépression majeure et manifestant des symptômes

psychotiques ou mélancoliques. La comparaison du début et de la fin du traitement révèle une réduction significative du temps de mouvement au-dessus du papier, ainsi qu'une diminution des effets de plus grande complexité sur le comportement moteur des patients. Tous ces résultats indiquent que la réduction du ralentissement psychomoteur à la fin du traitement est essentiellement due à une accélération des processus cognitifs. Le déficit moteur initial reste grosso modo inchangé et est en grande partie responsable de la différence entre le groupe des patients et le groupe de contrôle qui subsiste après le traitement. Les évolutions divergentes du ralentissement cognitif et du ralentissement moteur pendant le traitement, ont donné lieu à une analyse détaillée de ce ralentissement moteur même. Nous présentons cette étude dans le Chapitre 6.

Les dix épreuves utilisées dans cette étude sont décrites in extenso dans l'Appendice. Nous y exposons les résultats des 22 patients qui ont participé aux études antérieures, ainsi que les résultats de 8 patients impliqués dans la première étude (Chapitre 3). Ces épreuves motrices simples ne font pas appel à des processus cognitifs supérieurs; il en résulte un ralentissement évident, qui se manifeste dans des temps de mouvement plus longs et des vitesses d'exécution moins grandes. Un accroissement de l'amplitude des mouvements ou de l'exactitude requise entraîne une augmentation du ralentissement. Le ralentissement moteur était plus marqué pendant le premier quart des mouvements montants et descendants (hachurer) et pendant le dessin du premier trait dans la tâche Fitts', que dans le restant de la tâche. Ceci indique des difficultés dans la phase d'initiation. Même si des encouragements augmentaient la vitesse, la durée des mouvements restait toujours plus longue que celle de la moyenne des personnes de contrôle. Toutes ces caractéristiques indiquent des difficultés dans les processus de programmation sensori-moteur et, plus particulièrement, dans la phase d'initiation de l'exécution du mouvement. Ceci appuie les théories existantes sur le ralentissement global de toutes les actions en cas de dépression (par exemple par des problèmes d'activation), ainsi que les théories affirmant une relation intime entre les processus cognitifs et moteurs.

Dans le Chapitre 7, le ralentissement moteur lors des épreuves motrices simples, comme nous l'avons constaté au début du traitement, est comparé aux résultats à la fin du traitement. Dans la presque totalité des épreuves, le ralentissement des processus moteurs diminue entre T0 et T1. Cependant, des différences importantes entre les deux groupes subsistent. La réduction du ralentissement moteur se manifeste par une diminution des temps de mouvement et non pas par une augmentation des vitesses. Les temps de mouvement sont réduits parce que le nombre et la durée des pauses et des stops pendant le mouvement sont moins fréquents et moins longs, et parce que l'amplitude du mouvement est légèrement moins large. L'ensemble des caractéristiques du ralentissement à la fin du traitement est analogue à la situation initiale, décrite dans le chapitre précédent. Les caractéristiques sont généralement parlant identiques, mais les décalages entre les groupes sont plus petits ou ont même disparu. Reste la question de savoir si ce ralentissement moteur, qui a certes diminué mais qui n'a pas disparu après le traitement, doit être mis en rapport avec le "state" ou le "trait" du patient dépressif.

La discussion générale du Chapitre 8 offre une réflexion critique des études décrites dans cette thèse. Nous y évaluons les objectifs et nous discutons la méthode, la sélection des sujets, la procédure et le choix des tâches. Nous évaluons les résultats et nous questionnons la fiabilité et la validité des tâches d'écriture et de dessin. Finalement, nous discutons la spécificité des résultats et les implications pour la recherche future. Nos résultats sont compatibles avec l'hypothèse de Widlöcher et de Hardy-Bayle sur le dysfonctionnement global. Celui-ci provient d'un manque d'activation et d'initiation du mouvement et doit être mis en rapport avec la quantité d'effort requise par la tâche, quoiqu'elle se manifeste déjà dans des comportements dits "automatiques". Nos résultats confirment aussi que le ralentissement n'affecte pas directement la qualité de la prestation, mais bien la vitesse d'exécution. Par contre, nos résultats ne s'accordent guère avec les théories qui proposent une relation plus étroite entre les ralentissements moteur et cognitif. Ils mettent en évidence une évolution différente de ces 2 composantes au cours du traitement. Il résulte de la comparaison du début et de la fin du traitement, qu'un large

déficit moteur subsiste après le traitement, tandis que le ralentissement cognitif a quasi disparu. Nous discutons les implications de cette conclusion.

SAMENVATTING

Het onderwerp van dit proefschrift is psychomotorische vertraging bij depressieve patiënten. In de dagelijkse zorg voor depressieve patiënten worden psychomotorische veranderingen door de meeste psychiaters ervaren als een klinisch relevant symptoom of relevante symptomengroep met betrekking tot diagnose en behandeling. In sommige theorieën worden deze veranderingen zelfs als het kernsymptoom beschouwd van het depressieve syndroom in engere zin of van het melancholische en van het psychotische subtype.
Niettemin bestaat er geen éénduidige definitie van psychomotorische stoornissen bij depressie. Evenmin bestaat een helder inzicht in de cognitieve en motorische aspecten ervan. Het doel van de onderzoeken die in dit proefschrift worden beschreven, is de bijdrage te evalueren van een nieuwe methode tot de beschrijving van psychomotorische vertraging en van cognitieve en motorische componenten ervan bij depressieve patiënten. Deze methode bestaat uit het meten en het analyseren van fijn motorisch gedrag, dit zijn schrijf- en tekenbewegingen.

In hoofdstuk 2 wordt een literatuuroverzicht gegeven over de laatste vijftien jaren, van de meest gebruikte meetmethoden om psychomotorische vertraging bij depressieve patiënten te meten. De resultaten worden per methode samengevat: de scorings- en observatieschalen, het meten en het analyseren van specifiek nonverbaal gedrag, het spraakonderzoek, de eenvoudige en de keuzereactietijdmetingen, het onderzoek van de grove motoriek - vooral met behulp van actometrie -, en van de fijne motoriek. In de meeste onderzoeken is met behulp van deze methoden aangetoond dat depressieve patiënten als groep trager waren dan groepen van normale, gezonde controle-proefpersonen. Deze vertraging bleek - gedeeltelijk of volledig - van cognitieve aard te zijn. Of er ook een motorische vertraging optrad, is minder duidelijk. In de meeste onderzoeken waarin de effecten van behandeling met antidepressiva of met electroconvulsieve therapie werden gemeten, werd na behandeling wel een afname van de vertraging vastgesteld.

In hoofdstuk 3 worden de resultaten beschreven van de eerste twee studies, waaraan telkens 10 depressieve patiënten deelnamen. Hierin wordt de nieuwe methode beschreven om fijn motorisch gedrag te meten, met name het registreren en analyseren van schrijf- en tekenbewegingen met behulp van een schrijftablet, een speciaal daartoe ontworpen pen en een personal computer. De methode wordt tevens beschreven in de Appendix. Er werden zowel eenvoudige als complexe figuurkopieertaken toegepast. In vergelijking met groepen van voor leeftijd, sexe en opleiding gematchte, normale, gezonde controlepersonen, toonden de patiëntengroepen langere reactietijden (RT) en langere bewegingstijden (MT) bij het kopiëren van de eenvoudige figuren, en langere MT - vooral de bewegingstijden boven het papier - bij het kopiëren van de complexe figuren. Deze resultaten wezen op een duidelijke cognitieve component van de psychomotorische vertraging bij de patiënten. De afwezigheid van een verlenging van de RT bij het kopiëren van de complexe figuren, samengaande met het feit dat de patiënten meer fouten maakten en meer en langere reïnspecties nodig hadden dan de controlepersonen, wezen er op dat de patiënten een seriële strategie gebruikten in de uitvoering van deze taak. Een kleine groep van 6 patiënten werd een tweede maal getest, dit na behandeling met antidepressiva. De veranderingen in de Hamilton Depression Rating Scale (HDRS) tussen de twee afnamemomenten correleerden significant met de veranderingen van RT en MT bij het kopiëren van de eenvoudige figuren en met de veranderingen van MT bij het kopiëren van de complexe figuren. Dit wees er op dat het herhaaldelijk meten van tekenbewegingen bruikbaar kan zijn om psychomotorische veranderingen over de tijd heen te meten, evenals mogelijke effecten van behandeling.

Om deze eerste bevindingen te repliceren en verder te exploreren, werd een onderzoek opgezet, waarbij 22 klinische patiënten, lijdend aan een depressie in engere zin, getest werden bij het begin en bij het einde van een 6 weken durende behandeling met fluoxetine 20 mg. per dag. Ook 22 gezonde controle-proefpersonen namen aan het onderzoek deel. Er werd een brede waaier van taken uitgetekend om zoveel mogelijk aspecten van de psychomotorische vertraging van de patiënten te onderzoeken. Behalve zeer eenvoudige

motorische taakjes, waarbij geen beroep wordt gedaan op hogere cognitieve processen, werd ook een complexe rotatietaak met een hoge visuo-spatiële moeilijkheidsgraad opgezet.

In hoofdstuk 4 worden de resultaten samengevat van de figuur-kopieertaken bij het begin van de behandeling. Over het algemeen worden de eerdere bevindingen gerepliceerd. In alle taken werden bij de patiëntengroep significant langere RT en MT gemeten dan bij de controlegroep. Uit de analyses in de diverse taken van de RT, van de MT en van zijn componenten, en uit de cognitieve manipulaties tussen en binnen de opeenvolgende taken, bleek opnieuw duidelijk de vertraging van de cognitieve processen bij de patiëntengroep: langere RT bij de patiënten dan bij de controles in alle taken, langere pauzes op het papier gedurende de schrijfbeweging, evenals langere reïnspecties; tevens werden bij het kopiëren van de eenvoudige figuren significante interacties tussen groep en complexiteit gevonden.
De resultaten wezen tenslotte op een duidelijke motorische vertraging. Deze bleek vooral uit de langere bewegingstijden met de pen op het papier. Tussen de patiënten bestonden grote inter- individuele verschillen in graad van psychomotorische vertraging. Er werden geen correlaties gevonden tussen de kinematische variabelen en de schalen die de ernst van de depressie meten; de correlaties tussen de kinematische variabelen en de scores op de Salpêtrière Retardation Rating Scale waren zwak. Alhoewel effecten van de (co-)medicatie op de resultaten van de schrijf- en tekentaken niet konden uitgesloten worden, waren er geen argumenten voor een duidelijke invloed van het gebruik van medicijnen, in positieve, noch in negatieve zin. Of en welke veranderingen in deze cognitieve en motorische vertraging optraden, wanneer het begin (T0) en het einde (T1) van de behandeling werden vergeleken, wordt beantwoord in hoofdstuk 5.

Tussen T0 en T1 werd een significante afname van de RT vastgesteld in de hele patiëntengroep, en vooral in de subgroep van de patiënten die positief reageerden op de behandeling, dit zijn zij bij wie een daling van de HDRS van minimaal 40% optrad en de

HDRS-score op T1 maximaal 18 bedroeg. Het betrof 11 van de 21 patiënten, allen lijdend aan een depressie in engere zin met psychotische kenmerken, of van het melancholische subtype. Ook werd over het betreffende tijdsinterval een significante daling van de bewegingstijd boven het papier gemeten en een afname van de effecten van toenemende complexiteit op het motorische gedrag van de patiënten. Al deze resultaten gaven aan, dat de afname van psychomotorische vertraging na behandeling essentieel het gevolg was van een versnelling van de cognitieve processen. Het initieel motor deficit bleef ongewijzigd en was grotendeels verantwoordelijk voor het verschil op het einde van de behandeling tussen de patiënten- en de controlegroep. De verschillen in evolutie tussen de cognitieve en de motorische vertraging bij het begin en het einde van de behandeling waren aanleiding om de motorische vertraging zelf in detail te analyseren. Dit onderzoek wordt beschreven in hoofdstuk 6.

De tien trials, die in dit onderzoek werden gebruikt, staan nauwkeurig beschreven in de Appendix. Bij de resultaten van de 22 patiënten, die aan de vorige onderzoeken deelnamen, werden de resultaten gevoegd van 8 patiënten van het eerste onderzoek (hoofdstuk 3). In deze eenvoudige motorische taken, waarin geen beroep wordt gedaan op hogere cognitieve processen, bleek de vertraging duidelijk uit de langere bewegingstijden en de lagere snelheden. De vertraging nam toe bij een grotere amplitude van de beweging of wanneer een grotere nauwkeurigheid vereist was. De motorische vertraging was groter tijdens het eerste kwart van de arceerbewegingen en tijdens het neerzetten van telkens het eerste lijntje in de Fitts' taak, dan in de rest van de taak; dit duidde op moeilijkheden in de initiatiefase. Hoewel het stimuleren van de patiënt door de onderzoeker om de taak zo snel mogelijk uit te voeren effectief tot hogere snelheden leidde, bleven ook in deze conditie de bewegingstijden aanzienlijk langer. Het geheel van deze kenmerken wijst op problemen in de processen, betrokken in de sensori-motorische programmering, en meer specifiek in de startfase van de uitvoering van de beweging. Dit patroon bevestigt bestaande theorieën over de algehele vertraging van alle activiteiten in de depressie, door bijvoorbeeld een tekort aan activatie, alsook theorieën over het hechte verband tussen de cognitieve en de motorische processen.

In hoofdstuk 7 werd de vertraging in de eenvoudige motorische taken, zoals die werd vastgesteld bij het begin van de behandeling, vergeleken met de resultaten aan het einde ervan. De vertraging op T0 van de motorische processen, was op T1 in bijna alle trials verminderd; niettemin bleven er na behandeling grote verschillen bestaan tussen de beide groepen. De afname van de motorische vertraging bleek uit een afname van de bewegingstijden, niet uit een toename van de snelheden. De bewegingstijden waren korter omdat het aantal en de lengte van de pauzes en van de stops tijdens de beweging kleiner waren, en omdat de amplitude van de beweging enigszins afnam. Het patroon van de vertraging was op het einde van de behandeling analoog aan dat van het begin - zoals beschreven in het vorige hoofdstuk. De kenmerken waren over het algemeen dezelfde, maar de verschillen waren kleiner of zelfs verdwenen. Het blijft een vooralsnog onbeantwoorde vraag of deze motorische vertraging, die verminderde maar niet verdween na behandeling, moet opgevat worden als een 'state'- of als een 'trait'-gebonden kenmerk van de depressie.

De algemene discussie van hoofdstuk 8 bevat een kritische beschouwing over de beschreven onderzoeken. De doelstellingen worden geëvalueerd; de methode, de selectie van de proefpersonen, de procedure en de keuze van de taken worden besproken. De resultaten worden beoordeeld. De geldigheid en de betrouwbaarheid van de schrijf- en tekentaken worden bevraagd. Tenslotte komen de specificiteit van de resultaten en de implicaties voor toekomstig onderzoek aan de orde. Onze resultaten zijn compatibel met de hypothese van Widlöcher en Hardy-Bayle over een globale disfunctie, voortkomend uit een gebrekkige activatie en initiatie van de beweging en samenhangend met de hoeveelheid van 'effort' die de taak vraagt, maar die ook reeds optreedt in 'automatisch gedrag'. Ze stemmen tevens overeen met het besluit dat de vertraging primair niet de kwaliteit van de prestatie aantast, maar wel de snelheid van uitvoering. Daarentegen zijn onze resultaten in tegenspraak met hun opvatting over een nog hechtere band tussen de motorische en de cognitieve vertraging, dan over het algemeen wordt gedacht. Onze resultaten wijzen op een verschillende evolutie van deze componenten, wanneer het begin

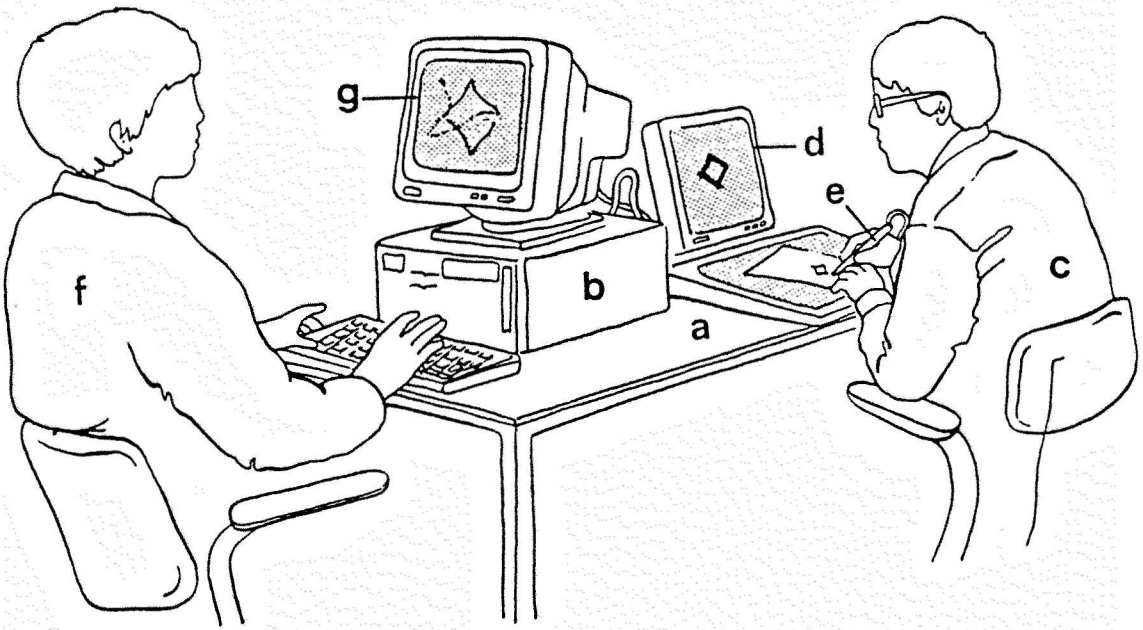
en het einde van de behandeling worden vergeleken. Hieruit bleek dat er een groot, alhoewel verminderd, motorisch defect bleef bestaan na de behandeling, terwijl de cognitieve vertraging bijna volledig was verdwenen. De implicaties hiervan worden besproken.

Appendix A

THE MEASUREMENT OF FINE MOTOR RETARDATION DURING WRITING AND DRAWING TASKS

In this Appendix (A) the test situation is described, (B) the general introduction to the test is shown, and in (C), (D) and (E) the instructions and the examples of Part I (speaking and writing), Part II (simple motor tasks) and Part III (figure copying tasks) are presented.

A. The test situation



The test situation is as follows: the subject (c) is copying a stimulus figure presented on his monitor (d) using a pen (e) and a graphics tablet (digitiser) (a). The figure disappears from the monitor as soon as the subject puts pen to paper. Using a personal computer (b), the researcher (f) can observe the movements made by the subject on the graphics tablet by means of his own monitor (g).

B. General introduction to the test

Welcome to the test, Miss, Mrs or Mr X, in which you have agreed to participate. We are delighted that you are willing to cooperate. The test takes about one hour to complete and consists of a number of simple drawing tasks - we are particularly interested in measuring how you normally draw and write. Measurements are recorded using the equipment in front of you: a personal computer, a graphics tablet (digitiser) and a pen to write or draw with. You will be asked to place a piece of paper on the graphics tablet and to write on it with the pen. Try it now to see how it feels. If the cable is in your way, don't be afraid to push it to one side.

Using a cassette recorder, we will record part of the test, in order to be able to play it back at a later stage.

If you normally wear reading glasses, then we recommend that you wear them for the test.

C. Part I: Writing and speaking

Task R1

To test the microphone and cassette recorder:

Counting: 1 2 3 4 5 6 7 8 9 10.

Instruction:

'We are now going to test the equipment; please count from 1 to 10 into the microphone.'

Task R2

Test the graphics tablet:

Writing: 1 2 3 4 5 6 7 8 9 10

Instruction:

'Please write all the numbers from 1 to 10 at the top of the paper'.

Task R3

Writing down the text that is dictated by the cassette player:

'We are not at home/ You can reach us after two o'clock/ Or leave your own telephone number so that we can ring you back'.

Instruction:

'You will hear a text recorded on tape. It is a practice text that might be used on an answering machine; the test does not apply in any way to you or to us.

Please write down the text on the paper. Do so in such a way that you can read it back to us later. The text will be dictated line by line. First of all, you will hear a voice counting from 1 to 8 so that you can adjust the volume...

Please start writing after you hear the beep.'

Task R4

Reading out the text that has just be written down.

Instruction:

'Please read the text that you have just written down into the microphone.'

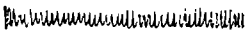
D. Part II: Simple motor tasks

Trial 1: Rapid up and down movements normal writing height and at the subject's own speed (clean sheet of paper).

Instruction:

'Please make rapid up and down movements with the pen on the paper of about the same height as your normal writing and at your own speed. An example is given below; as you can see, the peaks do not all need to be drawn neatly at the same height. Practice for a moment now.... Start after you hear the beep.'

Example:



Trial 2: Rapid up and down movements 3 x larger than in the preceding trial, at the subject's own speed (clean sheet of paper).

Instruction:

'Will you repeat the up and down movements, but make them three times larger than in the previous exercise. Look at the example. Start as soon as you hear the beep.'

Example:

Trial 3: Rapid up and down movements from small to large, at the subject's own speed (sheet with a vertical line, from small to large).

Instruction:

'Starting at the black dot, repeat the up and down movements at your normal writing

height and at your own speed, but as soon as you reach the vertical line, make the movements three times larger. Do not stop when you change the size of the movements. See the example below. Start as soon as you hear the beep.'

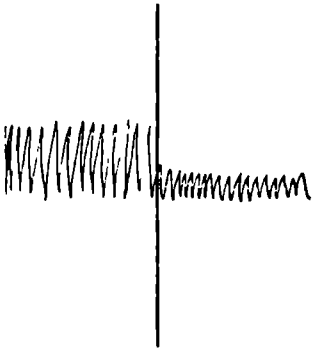
Example:

Trial 4: Rapid up and down movements from large to small at the subject's own speed (sheet with vertical line from large to small).

Instruction:

'Will you repeat the previous exercise, but this time start with the large movements until you reach the vertical line and then change to smaller ones. Do not stop when you change the size of the movements. Start as soon as you hear the beep.'

Example:



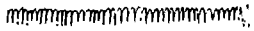
Trial 5: Rapid up and down movements as fast as possible (sheet with vertical line).

Instruction:

'Please make rapid up and down movements with the pen on the paper of about the same

height as your normal writing, but this time do it as fast as you can (see example). It does not matter if it looks more untidy. Start as soon as you hear the beep.'

Example:

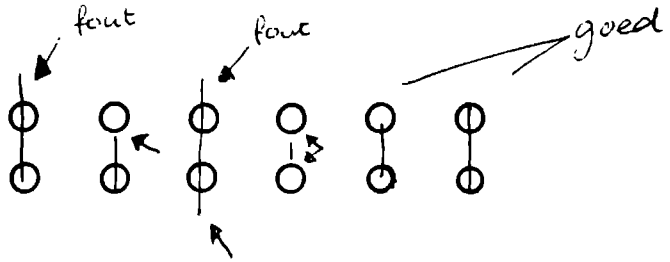


Trial 6: Drawing a line to connect two large circles together (sheet with circles).

Instruction:

'Below you can see a number of circles. Connect each pair together with a vertical line, so that the beginning of the line falls somewhere inside the top circle and ends somewhere inside the lower circle (see the example showing correct and incorrect lines). Please be as quick and as accurate as you can. Start as soon as you hear the beep.'

Example:



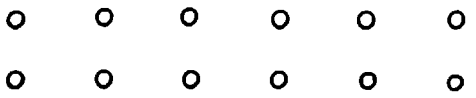
Trial 7: Drawing a line to connect two small circles together (sheet with small circles).

Instruction:

'Here are some more circles, but they are smaller than those in the previous exercise. Once again, connect each pair with a vertical line that starts inside the top circle and ends inside

the lower one. Please be as quick and as accurate as you can. Start as soon as you hear the beep.'

Example



Trial 8: The same as trial 7 (sheet with small circles).

Instruction:

'Please do the same as in the previous exercise.'

Trial 9: The same as trial 6 (sheet with large circles).

Instruction:

'Connect each pair of large circles together with a vertical line, in the same way as in the previous exercises. Start as soon as you hear the beep.'

Trial 10: Continue drawing lines at the subject's own speed (at least 10) (sheet with backslashes).

Instruction:

'Below a number of lines have been drawn in horizontal a line on the paper. Continue the line of backslashes until I tell you to stop. Start as soon as you hear the beep.'

Example: ////////

E. Part III: Figure copying tasks

Task C1

As quickly and as accurately as possible, copying 48 lines and simple figures that appear on the monitor (long strip of paper).

Instruction:

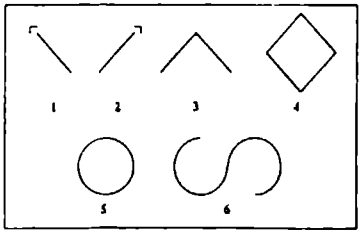
'In a moment you will see a series of simple figures on your monitor. Please copy them as *quickly* and as *accurately* as possible (just like copying the letters of the alphabet, as long as the figures are the same). As soon as you start drawing, the figure will disappear from the monitor.

First of all, you will be given three or four for practice. It is very important that you copy the figures in one go - in other words, do not go over the same line twice! If the pen does not seem to be writing clearly on the paper, that does not matter.'

After the practice figures (N=4):

'Do you understand what you have to do? You have been doing it correctly. Now we would like you to copy a whole series of figures. Remember, do not go over any of the lines twice! Are you ready?'

Figures used in the task:



Task C2

Copying 12 figures, of which 4 will be familiar, 4 unfamiliar and 4 letters as quickly and as accurately as possible.

Instruction:

'Please copy the figures shown on your monitor as quickly and as accurately as possible. The figure will disappear as soon as you start drawing. Some of the figures are a little more complicated than the previous ones. If you become well and truly stuck, you can recall the figure to the monitor by touching the pen against the red spot. Remember, only recall the figure if you are totally unable to continue! Once again, it is important that you do not go over any of the lines twice. If the pen does not seem to be writing clearly on the paper, that does not matter. First of all, you will be given three or four for practice.'

After the practice figures (N=4):

'If you understand what you have to do, we can start the exercise. There are fewer figures than in the previous assignment. Are you ready?'

Figures used at the start of therapy (T0)

Letters

4 8

Figuren

4 8

Patronen

4 8

Figures used at the end of therapy (T1)

Letters

4 8

Figuren

4 8

Patronen

4 8

Task C3

As quickly and as accurately as possible, drawing the 8 figures after rotating them through 90 degrees to the right (in other words, through one quarter turn) (4 letters/numbers and 4 corresponding unfamiliar figures).

Instruction:

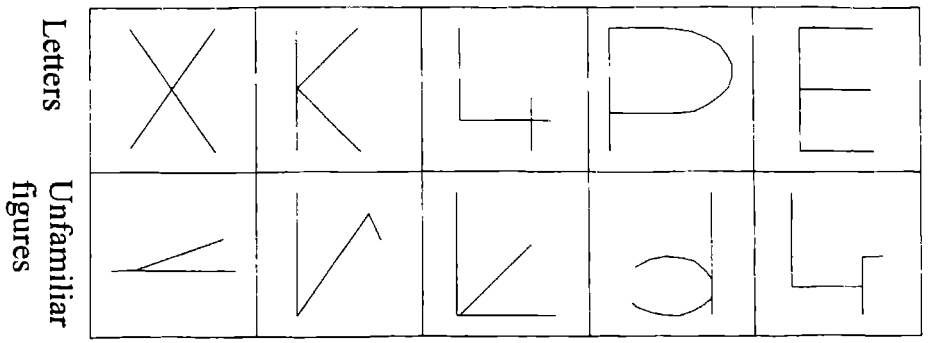
'In this part of the exercise, you are required to redraw the figure shown on your monitor after rotating it through 90 degrees to the right. Please do this as quickly and as accurately as possible. Here is an example (shown on paper).

Do you understand? First we will do one or two for practice. Look carefully at the figure before you start drawing, because as soon as you put pen to paper, the figure will disappear from your monitor. Once again, if you get really stuck, you can recall the figure to the monitor by touching the pen against the red spot. Only do this if you are totally unable to remember!'

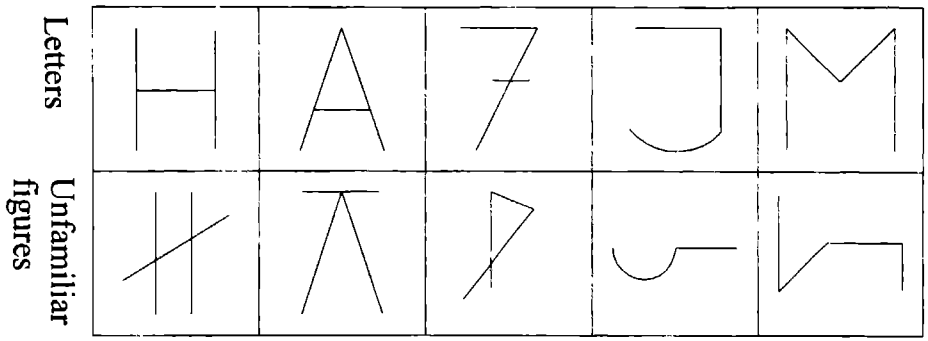
After the practice figures (N=2):

'Now we will begin. Are you ready?'

Figures used at the start of therapy (T0)



Figures used at the end of therapy (T1)



Task C4

Memory test: figures that were copied in task C2 have now been placed among a number of alternatives. The subject must indicate the correct figure as quickly as possible. First, 4 figures are shown among a series of others that bear a strong resemblance. In conclusion, 4 other figures are shown among 4 completely different figures. The latter forms an easy finishing task.

Instruction:

'In this exercise, you do not have to draw or write anything. During the past hour you have copied a fairly large number of figures. Some of these figures will now be shown among a number of other figures that you have not yet seen. Please indicate, as quickly as possible, which figure you have already seen. After my starting signal, press the middle button and hold it down for as long as you need to study the figures. Four figures will be shown on the monitor. Study the figures carefully, release the middle button and press the button that corresponds with the figure of your choice: choose from top left, top right, bottom left, bottom right. If you wish to correct your choice, you can do this yourself. You can recall the figures by pressing the middle button. First we will do three or four for practice.'

After the practice figures (N=4):

'Now we are ready to start. Only recall the figures if you think that you have made the wrong choice. Are you ready?' Press enter. 'Press the middle button and look carefully at the figures on your monitor.'

Task C5

Symbol Digit Substitution Task.

Instruction:

The material for this test is printed on the answer sheet. Place the test in front of the subject and say while you point to the key, 'Look at these boxes. In each one you can see a sign in the top half and a number in the bottom half. Under each sign there is a number. And here you can see (pointing to the examples) that there are signs in the upper boxes, but no numbers in the bottom boxes. It is your task to write the number that corresponds with the sign in each of the boxes, like this (pointing to the key and then to the examples). Here you can see this sign, so you have to fill in a number 2 (subject fills in a 2). Here you can see this sign, so you fill in a number 1 (subject fills it in). Here you can see this sign, so you fill in a number 3 (subject fills it in).

Give the subject a pencil to fill in the remaining 7 examples. Draw the subject's attention to the line that divides the examples and the actual test and say, 'fill in these examples up to this line.'

If the subject does not understand the exercise, help him with a few more examples until they have all been completed.

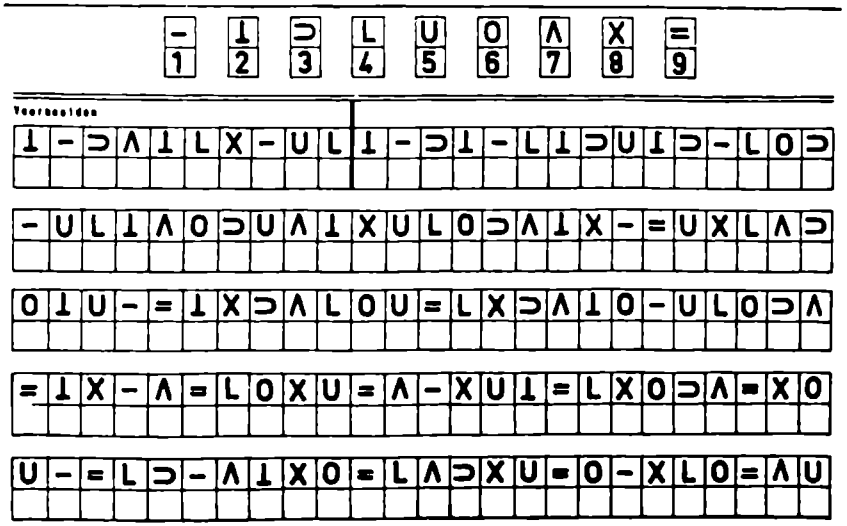
After the demonstration and practice session, point to the first box after the examples and say, 'When I give the start sign, start here and fill in as many boxes as you can without leaving any out. Are you ready? Start!'

If the subject starts to leave boxes out or only fills in one particular number, say to him, 'you have to fill them in one after the other, without leaving any out.'

Time limit: 90 seconds. The stopwatch is started as soon as the start sign is given, after completing the examples. The timing of this test is very strict.

Scoring: The researcher places the key on the test paper and awards one point for each correct answer. The first line has 15 boxes; the other lines have 25 boxes each.
Maximum score: 115 points

Symbol Digit Substitution Task

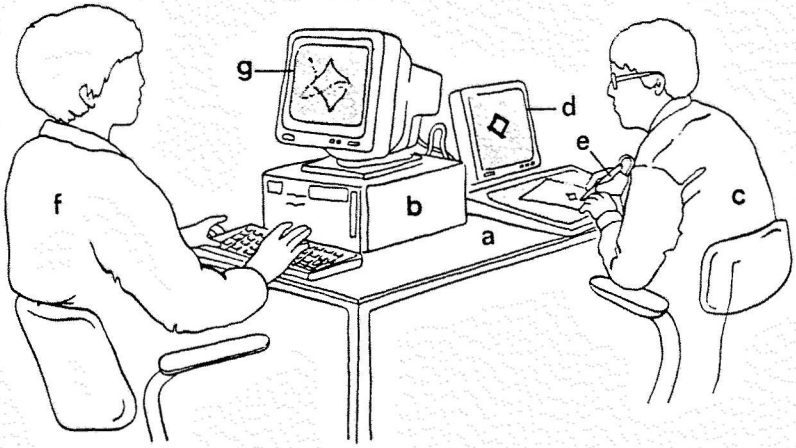


Appendix B

HET METEN VAN FIJN MOTORISCHE VERTRAGING TIJDENS SCHRIJF- EN TEKENTAKEN

Deze Appendix bevat de volgende onderdelen. In (A) wordt de testsituatie visueel voorgesteld. In (B) wordt de algemene inleiding op het onderzoek beschreven. In (C), (D) en (E) worden de letterlijke instructies en de voorbeelden van respectievelijk Deel I (Schrijven en Spreken), Deel II (Eenvoudige motorische taken) en Deel III (Figuur copieertaken) weergegeven. Voor een representatie van de voorbeelden en de figuurtjes van elke taak wordt de lezer verwezen naar Appendix A.

A. De testsituatie



De testsituatie is als volgt: de proefpersoon (c) copieert met behulp van een pen (e) en een schrijftablet (a) een figuurtje dat verschijnt op de monitor (d). Het figuurtje verdwijnt van het scherm zodra de proefpersoon de pen op het papier plaatst. Met behulp van een PC (b) observeert de onderzoeker (f) op zijn eigen monitor (g) de bewegingen die de proefpersoon op het schrijftablet maakt.

"Welkom Mevrouw, Meneer X. U heeft uw toestemming gegeven om deel te nemen aan dit onderzoek. We vinden het heel plezierig dat u heeft willen meewerken. Het onderzoek duurt ongeveer een uur en bestaat uit een aantal eenvoudige taken, waarbij we vooral meten hoe u normaal tekent en schrijft. Dit gebeurt door middel van deze apparatuur, met name een computer en een schrijftablet waarop u met deze pen kunt schrijven. De bedoeling is dat u schrijft op een stuk papier, dat u op het tablet legt. Probeert u het maar eens, dan merkt u hoe het voelt. Als het snoer in de weg zit, hangt u het dan gerust opzij. Met de cassetterecorder willen we *straks een testonderdeel opnemen*, zodat we dit later kunnen naluisteren.

Draagt u normaal een leesbril? Zo ja, dan is het nu ook goed om die op te zetten.

Deel I: Schrijven en spreken

Taak R1.

Uittesten microfoon/cassetterecorder.

Tellen: 1 2 3 4 5 6 7 8 9 10.

Instructie:

"Wij willen nu even het apparaat instellen. Wilt u in de microfoon van 1 tot en met 10 tellen?"

Taak R2.

Uittesten XY-tablet.

Schrijven: 1 2 3 4 5 6 7 8 9 10

Instructie:

"Wilt u bovenaan het papier de cijfers 1 tot en met 10 opschrijven?

Taak R3.

Het opschrijven van een tekst die via het bandje wordt gedicteerd:

"Wij zijn nu niet thuis/

U kunt ons wel bellen na twee uur/

Of geef uw eigen telefoonnummer/

zodat wij u zelf kunnen bellen".

Instructie:

"U krijgt via het bandje een tekst te horen. Dit is een voorbeeldtekst, die op een antwoordapparaat zou kunnen staan; de tekst heeft noch op u, noch op ons betrekking.
Ik zou u willen vragen deze tekst op papier te schrijven. Wilt u zó schrijven dat u het straks zelf kunt lezen? De tekst wordt regel voor regel gedicteerd. Er wordt eerst tot 8 geteld om het volume in te stellen....
U begint te schrijven nadat u de pieptoon heeft gehoord."

Taak R4.

Het inspreken van de zojuist opgeschreven tekst.

Instructie:

"Wilt u nu de geschreven tekst in de microfoon spreken"?

Deel II: Motorische taken

Trial 1: Het arceren op normale schrijfhoogte en in het eigen tempo (leeg blad).

Instructie:

"Ik zou u willen vragen of u eventjes gewoon van boven naar beneden op en neer wilt krassen, in het tempo dat u zelf het plezierigst vindt. Hier ziet u een voorbeeld van wat de bedoeling is. U ziet dat het niet netjes even hoog hoeft (probeert u maar even) .....Begint u na de piep".

Trial 2: Het arceren 3 x zo groot als bij de vorige trial, in eigen tempo (leeg blad).

Instructie:

"Wilt u nog eens krassen, maar dan drie keer zo groot? Kijkt u maar weer naar het voorbeeld.

Ook nu weer beginnen na de piep".

Trial 3: Het arceren van klein naar groot in eigen tempo (blad met balk van klein naar groot).

Instructie:

"Wilt u ook nu weer krassen, eerst bij de punt beginnen in gewone schrijfhoogte, maar bij de lijn doorgaan in 3 x zo groot? Dus niet stoppen wanneer u van grootte verandert. Kijkt u maar naar het voorbeeld.

Begint u maar na de piep".

Trial 4: Het arceren van groot naar klein in eigen tempo (blad met balk van groot naar klein).

Instructie:

"Wilt u dit nog eens doen maar dan bij de lijn van groot naar klein. U moet niet stoppen met krassen wanneer u van grootte verandert.

Begint u maar na de piep".

Trial 5: Zo snel mogelijk arceren (blad met balk).

Instructie:

"Wilt u nog eens krassen, ongeveer zo groot als de eerste keer (zie voorbeeld), maar dan zo snel mogelijk? Het is niet erg als het slordiger is.

Ook hier weer beginnen na de piep".

Trial 6: Grote cirkels met elkaar verbinden (blad met cirkels).

Instructie:

"U ziet hier een aantal cirkeltjes. Wilt u deze twee aan twee met verticale lijntjes aan elkaar verbinden, zodat het lijntje ergens binnenin het eerste cirkeltje start en ergens binnenin het tweede cirkeltje eindigt (Laat het voorbeeld zien: zo goed, zo niet goed). Wilt u het zo snel en zo goed mogelijk doen?

Begint u maar na de piep".

Trial 7: Kleine cirkels verbinden (blad kleine cirkels).

Instructie:

"Hier zijn nog een aantal cirkeltjes maar nu wat kleiner. Wilt u nog eens hetzelfde doen? De cirkeltjes twee aan twee met verticale lijntjes verbinden, zo dat het lijntje binnenin het bovenste cirkeltje start en binnenin het onderste cirkeltje eindigt. Zo snel en zo goed mogelijk.

Begint u maar na de pieptoon".

Trial 8: Hetzelfde als trial 7 (blad kleine cirkels).

Instructie:

"Deze doen we nog een keer".

Trial 9: Hetzelfde als trial 6 (blad met grote cirkels).

Instructie:

"Wilt u nu nog een keer de grote cirkels met elkaar verbinden".

Trial 10: Streepjes continueren in eigen tempo (minstens 10) (blad met streepjes).

Instructie:

"U ziet hier enkele streepjes: wilt u de regel met streepjes verder schrijven totdat ik "stop" zeg.

Begint u maar na de piep".

Taak C1

48 eenvoudige figuurtjes die op de monitor verschijnen zo snel mogelijk natekenen.

Bij deze test wordt een lange reep papier gebruikt.

Instructie:

"U zult zodadelijk eenvoudige figuurtjes op het scherm zien. De vraag aan u is om deze figuurtjes zo snel en zo goed mogelijk na te tekenen (net als een letter naschrijven, dus als er maar hetzelfde staat). Zodra u begint met tekenen verdwijnt het figuurtje van het scherm.

We zullen er eerst een paar doen om te oefenen.

Het is heel belangrijk dat u de figuurtjes in één keer tekent. Dus niet twee keer over eenzelfde lijn trekken! Als de pen wat onduidelijk op het papier schrijft is dat niet zo erg.

Na de proeftrials (N=4):

"Begrijpt u wat de bedoeling is? U doet het zo goed. We gaan nu een hele reeks figuurtjes natekenen. Teken de figuurtjes zonder overtrekken van lijntjes!

Bent u klaar?"

Taak C2

Het natekenen van 12 figuurtjes, waarvan 4 bekend, 4 onbekend en 4 letters.

Instructie:

"Bij deze tekentest is de vraag opnieuw de figuurtjes zo snel en zo goed mogelijk na te tekenen. Het figuurtje verdwijnt ook weer wanneer u begint met tekenen. De figuurtjes zijn soms iets moeilijker. Wanneer u het écht niet meer weet kunt u het figuurtje weer op het scherm laten verschijnen door met uw pen op het rode vlakje te tikken. U mag dat alleen maar doen wanneer u het écht niet meer weet. Ook hierbij geldt: de lijntjes niet meerdere malen overtrekken. Als de pen wat onduidelijk op het papier schrijft is dat niet zo erg. We zullen er weer eerst een paar oefenen."

Na de proeftrials (N=4):

"Wanneer u het begrepen heeft kunnen we nu echt beginnen. Het zijn nu minder figuurtjes dan de vorige keer.

Bent u klaar?

Taak C3

Het 90 graden naar rechts kantelen van 8 figuren (4 letters/cijfers en 4 afgeleide onbekende figuren).

Instructie:

"Bij dit onderdeel is het de bedoeling dat u het figuurtje dat op het scherm verschijnt zo snel en zo goed mogelijk natekent, maar dan 90 graden, ofwel een kwartslag naar rechts gekanteld.

Dus als voorbeeld: (geef een voorbeeld op papier).

"Begrijpt u het? Zullen we er dan nog één vanaf het scherm oefenen? Kijk goed totdat u weet hoe u het figuurtje moet tekenen, want als u begint met tekenen verdwijnt het figuurtje weer van het scherm. Ook bij deze taak kunt u het figuurtje weer tevoorschijn halen door op het rode vlakje te tikken met de pen. Doet u dat alleen wanneer u het echt niet meer weet".

Na de proeftrials (N=2):

"Nu beginnen we echt. Bent u klaar"?

Taak C4

Geheugentaak: figuurtjes die eerder in test C2 zijn nagetekend worden nu aangeboden temidden van alternatieven.

De vraag is zo snel mogelijk het juiste figuurtje aan te geven. Eerst worden 4 figuurtjes getoond temidden van sterk gelijkende figuurtjes. Als slot worden 4 andere figuurtjes getoond temidden van 4 sterk verschillende figuurtjes. Dit laatste is dan een gemakkelijke taak als slot.

Instructie:

"Als laatste doen we een taakje waarbij u niet hoeft te tekenen. U heeft het afgelopen uur een aantal figuurtjes moeten natekenen. Een aantal van die figuurtjes krijgt u nu weer te zien temidden van andere figuurtjes die u nog niet gezien heeft. Wilt u zo snel mogelijk aangeven welk figuurtje u al eerder heeft gezien? Na mijn startsein drukt u de middenknop in en houdt hem ingedrukt zolang u nodig hebt om te kijken. U ziet dan 4 figuurtjes op het scherm. Kijkt u goed en laat de middenknop los en druk op de knop die volgens u bij het juiste figuurtje hoort. Linksboven is deze knop, rechtsboven die, linksonder deze knop en rechtsonder die. Wanneer u denkt dat uw keuze fout was dan kunt u zichzelf verbeteren. U kunt de 4 figuurtjes nog terughalen door weer de middenknop in te drukken.

We zullen eerst even oefenen".

Na de proeftrials (N=4):

"Nu gaan we echt beginnen. Kijkt u alleen terug als u denkt dat uw keuze fout is. Bent u klaar"? Na enter: "Drukt u de middenknop maar in en kijkt u goed".

Taak C5

Symbol Digit Substitution Task.

Instructie:

Het materiaal voor deze test staat op het antwoordformulier. Leg de test vóór de proefpersoon en zeg, terwijl u de "sleutel" aanwijst, "kijk eens naar deze hokjes. U ziet telkens in de bovenste helft een teken staan en een cijfer in de onderste helft. Onder elk teken staat een ander cijfer. En hier ziet u (wijzend op de voorbeelden) dat de bovenste hokjes tekens hebben, maar de onderste hebben geen cijfer. U moet nu in elk van die hokjes het cijfer zetten dat bij het teken hoort, zo dus (wijzend op de sleutel en dan op de voorbeelden). Hier staat dit teken, dus moet u het cijfer 2 invullen (de proefleider vult het cijfer in). Hier staat dit teken, dus zet u dan een 1 (de proefleider vult in). Hier staat dit teken, dus u zet een 3 (de proefleider vult in).

Geef de proefpersoon dan een potlood om hem de 7 overgebleven voorbeelden te laten maken. Wijs de lijn aan, die de voorbeelden van de eigenlijke test scheidt, en zeg "doe het

nu bij deze tekens tot aan deze lijn".

Als de proefpersoon de opgave niet begrijpt, help hem dan nog met enkele voorbeelden, tot deze alle afgewerkt zijn.

Wijs na de demonstratie en de oefening, op het eerste hokje naar de voorbeelden en zeg: "als ik zeg dat u kunt beginnen, dan begint u hier en vult u zoveel hokjes in als u kunt, zonder er één over te slaan. Klaar? Begin".

Als de proefpersoon hokjes begint over te slaan of slechts één soort van cijfer begint in te vullen, zeg dan: "u moet ze op volgorde doen en er geen overslaan".

Tijdlimiet 90 seconden. De tijd begint te tellen zodra het beginsein gegeven is na het invullen van de voorbeelden. Bij deze test moet de tijd nauwkeurig in acht worden genomen.

Waardering De proefleider legt de sleutel op het testformulier en geeft 1 punt voor elk juist ingevuld cijfer. De eerste lijn telt 15 hokjes, de volgende lijnen elk 25.

Maximum-uitslag: 115 punten.

Dankwoord

Het schrijven van dit proefschrift was voor mij een avontuur, dat zich vooral afspeelde in het avonduur, wanneer het licht over de stad verflauwde, terwijl de uilen van Minerva hun vleugels erover uitsloegen. Het is het uur waarin ik als adolescent gefascineerd opging in de reizen van de Nautilus van Jules Verne of de tochten van de witte walvis van Herman Melville. Het verrichten van dit wetenschappelijk werk heeft dikwijls associaties hieraan opgeroepen. Immers voor de vooral psychotherapeutisch georiënteerde psychiater die ik was, was deze wereld van biologisch psychiatrisch onderzoek onontdekt gebied. Aan deze ontdekkingsreis heb ik veel plezier beleefd. Hiervoor ben ik veel dank verschuldigd aan mijn reisgenoten: Prof. Dr. F.G. Zitman voor zijn niet-aflatende inzet en zijn gedegen analyses van de reisverslagen; Dr. J.J.M. van Hoof voor het aanwijzen van de sporen en van de interessante gebieden, en voor zijn enthousiaste doorzetten bij het vervolgen van de tocht; Dr. W. Hulstijn, mijn trouwste reisgezel, ben ik bijzonder erkentelijk voor het uitstippelen en het plannen van de tocht, het evalueren en het analyseren van de vondsten en het helpen opstellen van de reisrapportages. Alle drie hebben ze mij geholpen om de reiskaarten te ontcijferen en de diepteboringen uit te voeren. Ik hoop dat de aldus gegroeide samenwerking blijvend zal zijn bij nieuwe en verdere reizen.

De patiënten en de medewerkers van de afdeling (hoofd: Prof. Dr. F.A.M. Kortmann) en in het bijzonder van de kliniek (chef patiëntenzorg: Drs. M.G. Nijs) Psychiatrie van het Academisch Ziekenhuis Nijmegen dank ik voor hun actieve deelname aan het onderzoek. Vele (studenten)psychologen, verbonden aan het NICI waren bij dit onderzoek betrokken: hun namen staan vermeld bij de betreffende hoofdstukken. De firma Eli Lilly heeft de opzet en de voortgang van dit onderzoek financieel ten dele ondersteund. Mevrouw J. Abma-Hill en mevrouw H. Meulenbroek-van der Meulen zeg ik dank voor het excellente Engelstalige correctie- en vertaalwerk van hoofdstuk 1, 4-8, appendix en summary, respectievelijk van de hoofdstukken 2 en 3. Mevr. E. van Bergen ben ik erkentelijk voor de onvermoeibaarheid en het goed humeur bij het (her)tikken van de manuscripten. De

romanschrijvers en de poëten, van wie de schrijfbewegingen in audioboeken zijn vastgelegd, dank ik voor hun gezelschap tijdens lange autoritten.

Mijn betrokkenheid in dit onderzoek werd in sterke mate gevoed door de dagelijkse klinische praxis. Het team van Fase B, Psychiatrisch Centrum Sint-Norbertushuis te Duffel, ben ik erkentelijk voor de loyale en creatieve samenwerking van elke dag. De collegae van het Psychiatrisch Centrum St. Norbertushuis en van de Universitaire Psychiatrische Centra van de U.Z. Leuven, alsook de Directies en de Raden van Beheer van beide ziekenhuizen, de Raad van Beheer van de VZW Gezondheidszorg Covabe wil ik bedanken voor de plaats en de functies die zij mij in hun midden hebben toevertrouwd. De samenwerking met Mevr. M. Heireman, co-opleider familietherapie te Leuven, is vriendschap geworden. Zij - teveel om op te noemen - die mij in het vak opgeleid en gevormd hebben zeg ik graag dank voor het boeiende geschenk dat zij mij gegeven hebben: een wellicht levenslange fascinatie voor het vak psychiatrie.

Als familietherapeut besef ik misschien meer dan anderen, dat wie ik ben, de systemische plaats die ik bezet, nauw samenhangen met transgenerationele loyaliteiten en contexten. Ik koester de herinnering aan twee creatieve grootvaders en twee levenskrachtige grootmoeders. Aan mijn goede en rechtschapen ouders en aan mijn lieve zus ben ik onzegbaar veel dank verschuldigd. Met de vrouw die ik lief heb, heb ik veel lief, maar ook groot leed gedeeld: zij heeft mij gesteund om troost te zoeken in dit werk. Tot slot noem ik mijn kinderen. Het plezier dat zij mij elke dag opnieuw geven weerspreekt elke motorische vertraging: kraaien en rennen vormen een waar motorisch genot.

Curriculum vitae

De schrijver van dit proefschrift werd geboren op 13 februari 1954 te Kuurne (België). In 1972 behaalde hij het diploma van het Middelbaar Onderwijs, Latijn-Wetenschappen aan het Sint- Amandscollege te Kortrijk. Van 1972 tot 1979 studeerde hij geneeskunde aan de Katholieke Universiteit Leuven, het kandidaatsgedeelte in de afdeling Kortrijk, het doctoraatsgedeelte in Leuven. Van 1 augustus 1979 tot 31 juli 1984 specialiseerde hij zich in de neuropsychiatrie in de Universitaire Psychiatrische Centra te Leuven (Prof. Dr. G. Buyse) en de afdeling Neurologie van het Universitair Ziekenhuis Sint-Rafaël te Leuven (Prof. Dr. R. Van den Bergh). Hij bekwaamde zich in meerdere psychotherapeutische richtingen, onder meer de cliëntgerichte psychotherapie, de hypnotherapie, de sexuele therapie en de partnerrelatie- en gezinstherapie. In 1984-1985 vervulde hij zijn militaire dienstplicht, waarna hij als psychiater werkte in het Centrum voor Geestelijke Gezondheidszorg Aeneas te Strombeek-Bever en het Communicatiecentrum, Universitair Ziekenhuis Salve Mater te Lovenjoel-Bierbeek. Vanaf 1 september 1986 tot heden is hij als universitair docent/psychiater werkzaam op de afdeling Psychiatrie van het Academisch Ziekenhuis Nijmegen, sinds 1 juli 1990 in deeltijd (achtereenvolgens: Prof. Dr. G.J. Zwaniken; Prof. Dr. F.A.M. Kortmann). Zijn voornaamste functie vervult hij vanaf dan in het Psychiatrisch Centrum Sint-Norbertushuis te Duffel, waar hij als psychiater-teamleider werkt in de Kliniek voor Opname en Kortdurende Psychiatrische Behandeling, de Fase; hij is er tevens als lesgever verbonden aan de Katholieke Hogeschool te Mechelen. Sinds 1 oktober 1993 is hij opleider in de familietherapie aan het Communicatiecentrum te Lovenjoel-Bierbeek, Universitaire Psychiatrische Centra (Prof. Dr. P. Igodt), in de functie van geneesheer-consulent van de Universitaire Ziekenhuizen Leuven.

STELLINGEN

behorende bij het proefschrift

IN SLOW MOTION

Cognitive and motor retardation during writing and drawing tasks in depressed inpatients.

Bernard G.C. Sabbe

I. Registrering en analyse van schrijf- en tekenbewegingen zijn een bruikbare methode om psychomotorische vertraging te meten bij depressieve patiënten (dit proefschrift).

II. Hoewel cognitieve en motorische processen moeilijk te scheiden zijn en beiden vertraagd zijn bij depressieve patiënten, heeft het toch zin ze te onderscheiden (dit proefschrift).

III. De bewering dat psychomotorische, d.i. cognitieve én motorische vertraging, verdwijnt na behandeling, zoals vastgesteld met behulp van onder meer spraakonderzoek en onderzoek van de grove motoriek, is onjuist (dit proefschrift).

IV. Stelling III bevestigt stelling II (dit proefschrift).

V. Het is vooralsnog onduidelijk welke van de variabelen snelheid, duur of afstand, de depressieve patiënten trachten te controleren om te versnellen of voor de vertraging van hun bewegingen te compenseren (dit proefschrift).

VI. De ene vertraging is de andere niet (Hulstijn, 1996; Van Hoof e.a., 1997).

VII. De initiatiemoeilijkheden van depressieve patiënten zijn van een andere aard dan de bekende startmoeilijkheden van de patiënt met morbus Parkinson (lopend onderzoek).

VIII. De uitspraak dat depressieve patiënten een depressieve stemming hebben, kan ernstig verdacht worden van "tautologein" (Widlöcher, 1986). Zij dient daarom als voorwerp van studie van de werkgroep "Les empêcheurs de penser en rond". Dit zou kunnen uitmonden in het advies: "Er moet sneller naar vertraging gekeken worden".

IX. Psychomotor symptoms in depression may have unique significance. They have high discriminative validity, may be the only symptoms of depression that distinguish depression subtypes, and are predictive of good response to tricyclic antidepressants (Sobin C, Sackeim HA, Am J Psychiatry 1997; 154: 4).

X. Schrijven is fundamenteel anders dan spreken: "Ecrire est hurler sans bruit". Het leidt tot eenzaamheid en tot de ontdekking dat stilte enkel bestaat binnenshuis, wanneer je er alleen bent (naar Marguerite Duras in "Ecrire").

XI. Het in de actuele socio-culturele context opvoeden van 4 kinderen door 2 buitenshuis werkende ouders, is een existentiële ervaring van het gefragmenteerde van het postmoderne bestaan.

XII. De angelsaksische uitspraak "hub a pub grub" wordt door de meeste onderdanen van het koninkrijk België te weinig gesmaakt. Ze is evenmin te vertalen door een broodje gezond.

XIII. Mourons pour des idées, mais de mort lente (Georges Brassens).

XIV. Van de oogarts kan de psychiater leren dat over de oogbol een tranenfilm moet liggen om scherp te kunnen zien.