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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. © 1997 Elsevier Science B.V.

1. Introduction

Interest in psychomotor retardation as an important or even core symptom of the depressive syndrome (Widlöcher and 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 and Paykel, 1989; Browning and Cowen, 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 et al., 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

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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 Section 2 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., submitted). 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.

2. Methods

2.1. 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.

2.2. 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 6 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 (Fig. 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 (±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 ±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 ±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.

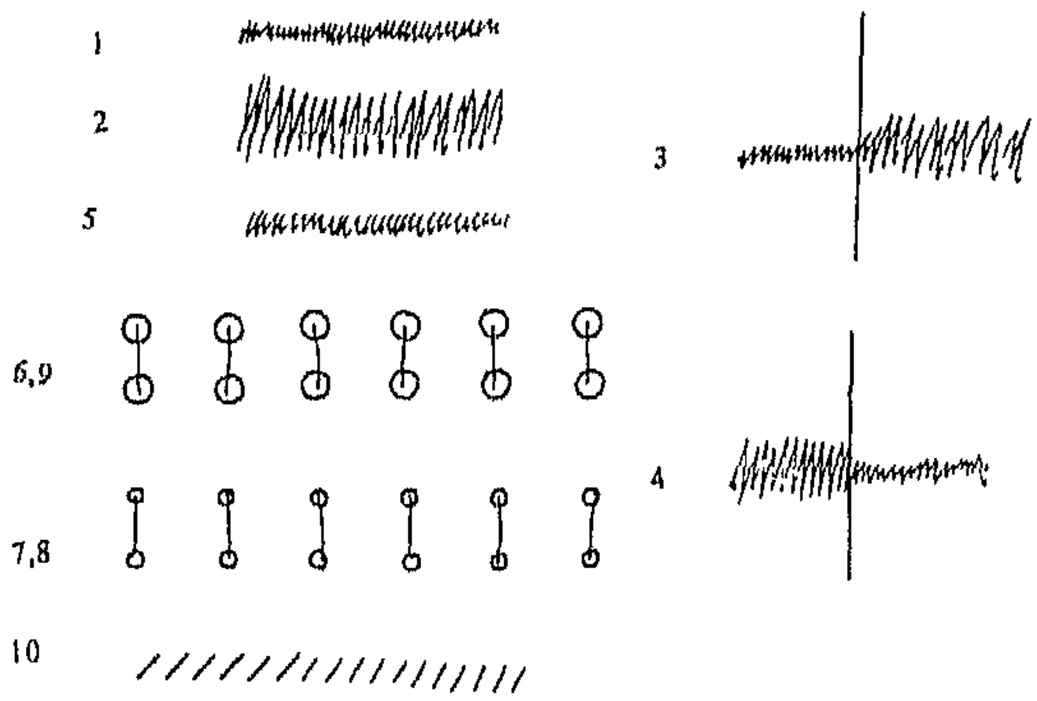

Fig. 1. Stimulus designs used in trials 1 to 10.

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 min. 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.

2.3. 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 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.

3. Results

3.1. 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) ($p = .000$) on the Hamilton Depression Rating Scale, 59.2 (S.D.: 10.4) and 50.9 (S.D.: 14.8) ($p = .001$) on the Zung Self Rating Scale and 24.5 (S.D.: 7.2) (Zung, 1965) and 18.2 (S.D.: 11.7) ($p = .01$) for the Salpêtrière Retardation Rating Scale.

3.2. Drawing tasks: General remarks

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 Fig. 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 Fig. 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; $F = 4.09$, $df = 1, 42$, $p = 0.05$).

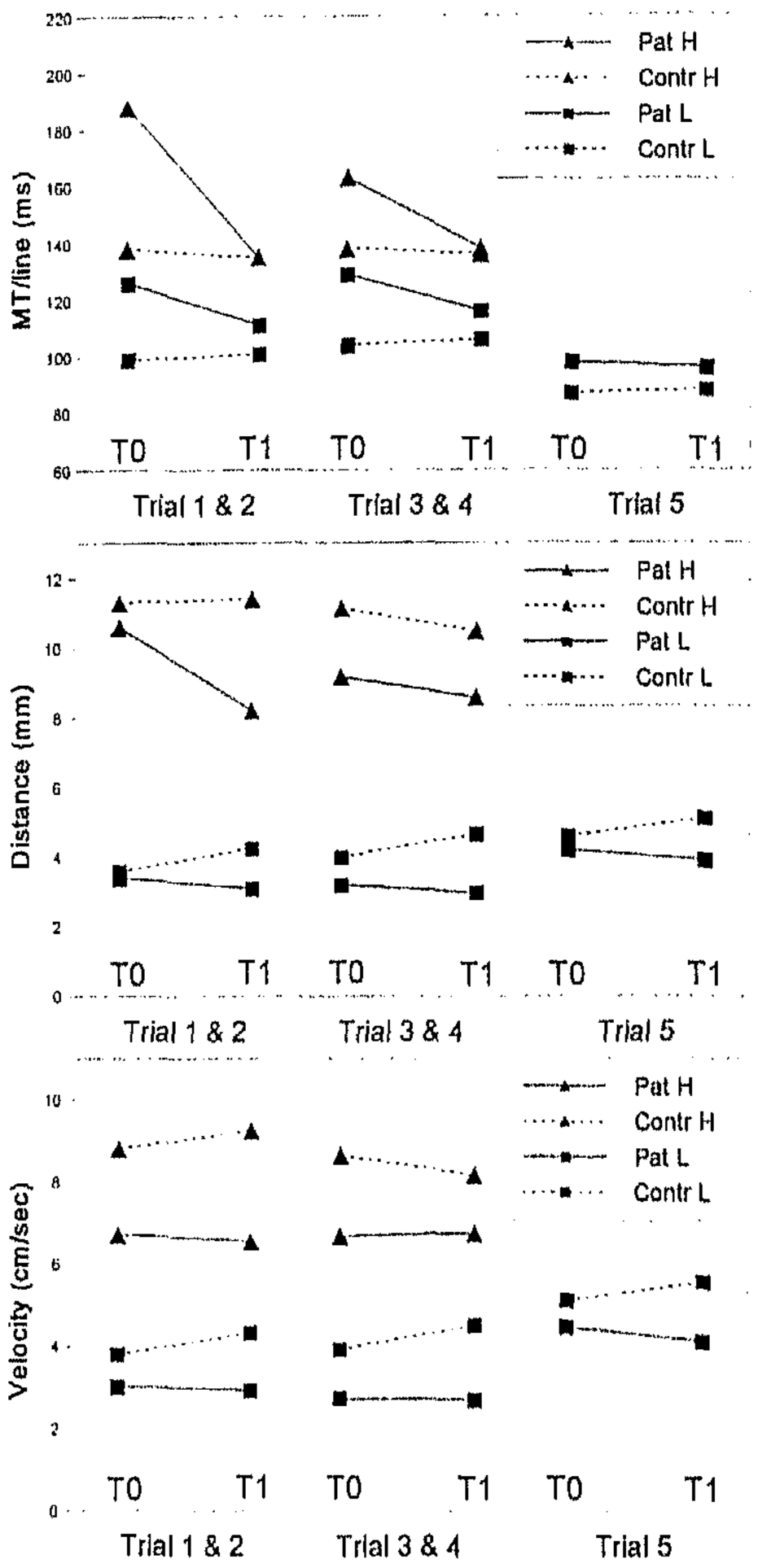

Fig. 2. Mean movement times (MT) per line (upper panel), mean distances per line (middle panel) and mean velocities (Vel) per line (lower panel) of the depressed patients and the controls at the start (T0) and end (T1) of treatment for trials 1 and 2, 3 and 4 and 5. L = low amplitude movements; H = high amplitude movements.

3.3. Start of treatment

At the start of treatment (T0) (Figs. 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

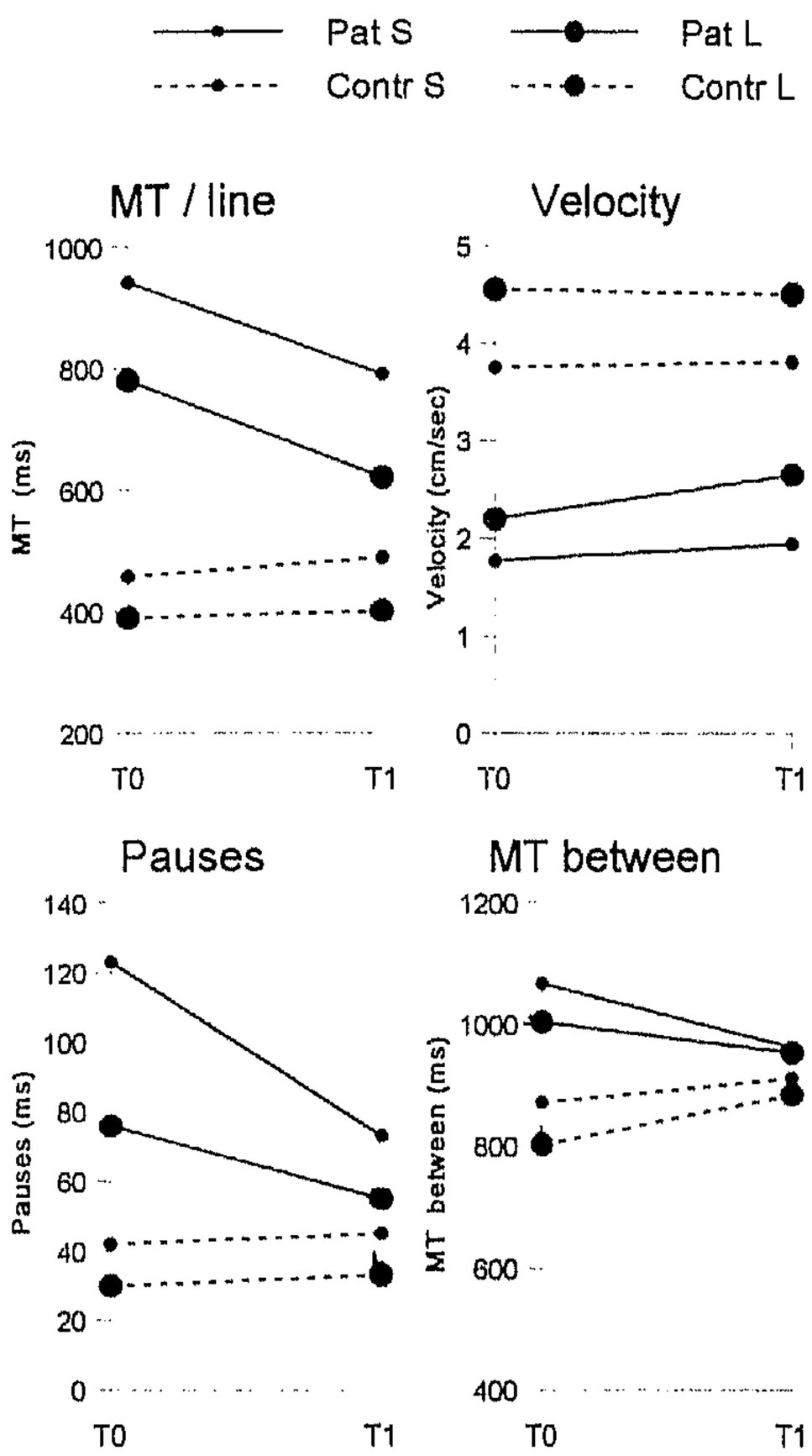

Fig. 3. Mean movement times (MT) per line (upper left panel), mean velocities (Vel) per line (upper right panel), mean pauses (Pauses) per line (lower left panel) and mean movement times between lines (MT between) per line (lower right panel) of the depressed patients and the controls at the start (T0)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

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.

3.4. 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 Figs. 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 and 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 (Fig. 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 (Fig. 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 (Fig. 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 (Fig. 2, lower panel; Fig. 3, upper right panel) was nearly the same at T0 and T1 and remained far lower at T1 than that of the control group.

3.5. 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).

3.5.1. Amplitude

Amplitude was manipulated in trials 1 to 4. Compare the upper lines (high amplitude) and lower lines (low amplitude) in Fig. 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.

3.5.2. Accuracy

Accuracy demands were manipulated in trials 6 to 9. Compare the lines between large targets and the lines between small targets in Fig. 3. (MT: upper left

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 and 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 and 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*

#$p < 0.10$, *$p < 0.05$, **$p \leq 0.01$, ***$p \leq 0.001$

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: $F = 5.09$, $df = 1, 42$, $p = .029$ and for Pauses per line: $F = 4.66$, $df = 1, 42$, $p = .037$). 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: $F = 8.13$, $df = 1, 42$, $p = .007$) and for Pauses per line it disappeared ($F = .39$, $df = 1, 42$, $p = .536$).

3.5.3. 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 (Fig. 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.

3.5.4. 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, $p = .029$ and trial 2: $F = 2.30$, $df = 3$, 126,

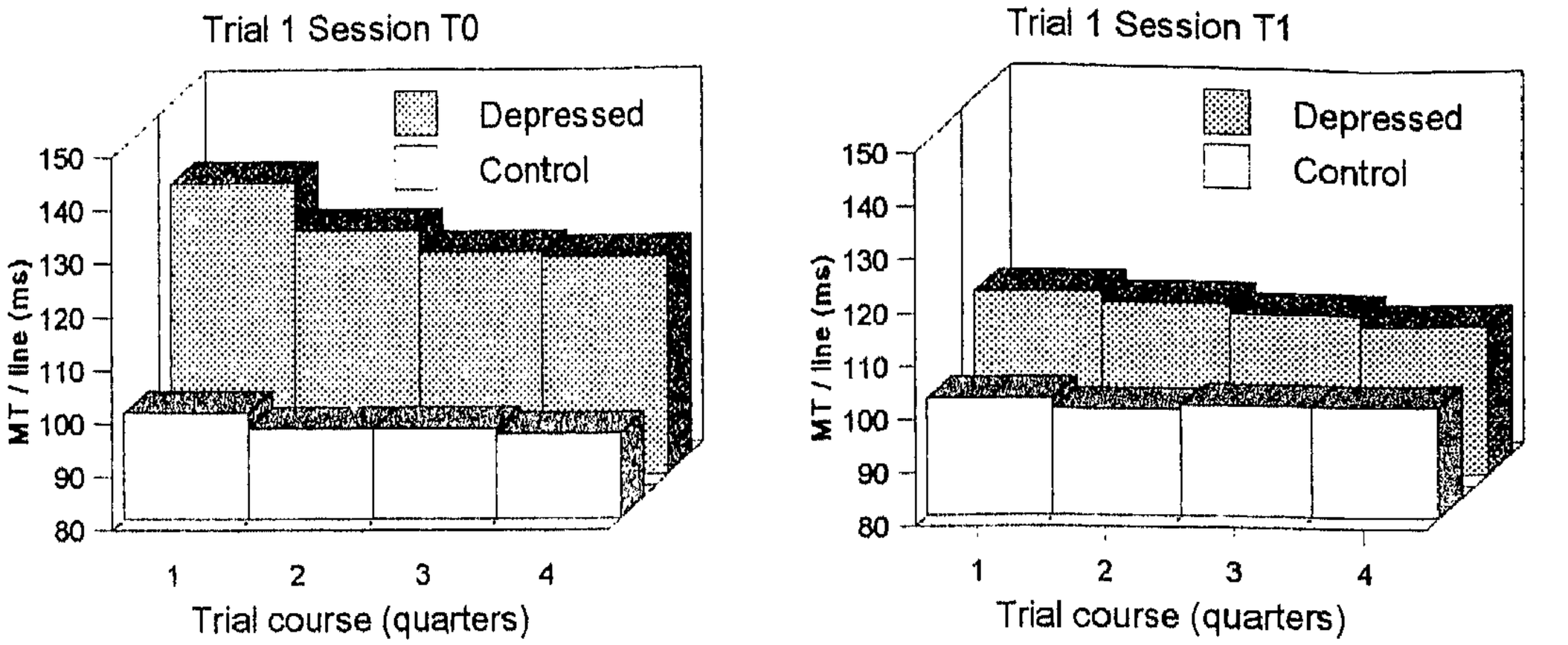

Fig. 4. Mean movement times (MT) per line of the depressed patients and the controls at the start (T0) (left panel) and end (T1) (right panel) of treatment for each quarter of trial 1 separately.

$p = .080$) (for trial 1 see Fig. 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: $F = 3.39$, $df = 1, 42$, $p = .073$) (Fig. 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: $F = 1.15$, $df = 3, 126$, $p = .334$ and trial 2: $F = 1.06$, $df = 3, 126$, $p = .367$) (for trial 1 see Fig. 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: $F = 0.00$, $df = 1, 42$, $p = .963$) (Fig. 5, right panel).

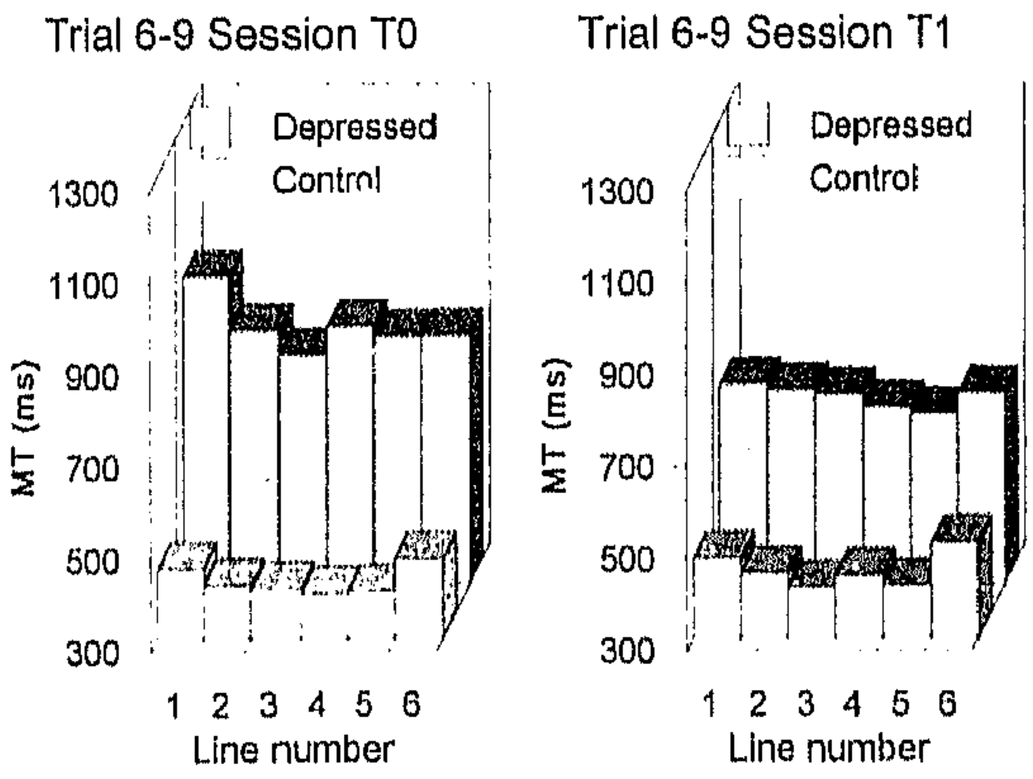

Fig. 5. Mean movement times (MT) per line of the depressed patients and the controls at the start (T0) (left panel) and end (T1) (right panel) of treatment for each line of trials 6 to 9 separately.

4. Discussion

In this study we compared the degree and the pattern of motor slowing between a group of in-patients with a Major Depressive Episode and 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,b) and we designed very simple drawing tasks that mainly draw on motor control processes of sensori-motor 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., submitted).

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., submitted) 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 refine 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, 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, 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. Fur-

ther 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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References

American Psychiatric Association (1987) Diagnostic and statistical manual of mental disorders, 3rd ed. – revised. American Psychiatric Association, Washington DC.

Browning, S.M. and Cowen, P.J. (1986) Changes in mood, appetite and psychomotor retardation in depressed patients given ECT. Br. J. Psychiatry 149, 371–373.

Flint, A.J., Black, S.E., Campbell-Taylor, I., Gailey, G.F. and Levinton, C. (1993) Abnormal speech articulation, psychomotor retardation, and subcortical dysfunction in major depression. J. Psychiatric Res. 27, 309–319.

Ghozlan, A. and Widlöcher, D. (1987) Epreuves cognitives et ralentissement psychomoteur dépressif. J. Psychiat. Biol. Thérap. 25, 14–17.

Ghozlan, A. and Widlocher, D. (1989) Decision time and movement time in depression: Differential effects of practice before and after clinical improvement. Percept. Mot. Skills 68, 187–192.

Godfrey, H.P.D. and Knight, R.G. (1984) The validity of actometer and speech activity measures in the assessment of depressed patients. Br. J. Psychiatry 145, 159–163.

Greden, J.F. and Carroll, B.J. (1980) Decrease in speech pause times with treatment of endogenous depression. Biol. Psychiatry 15, 575–587.

Greden, J.F., Albala, A.A., Smokler, I.A., Gardner, R. and Carroll, B.J. (1981) Speech pause time: a marker of psychomotor retardation among endogenous depressives. Biol. Psychiatry 16, 581–589.

Hardy, P., Jouvent, R. and Widlöcher, D. (1984) Speech pause time and the Retardation Rating Scale for depression. Towards a reciprocal validation. J. Affect. Disord. 6, 123–127.

Hamilton, M. (1960) A rating scale for depression. J. Neurol. Neurosurg. Psychiatry 23, 56–62.

Hoffmann, G.M.A., Gonze, J.C. and Mendlewicz, J. (1985) Speech pause time as a method for the evaluation of psychomotor retardation in depressive illness. Br. J. Psychiatry 146, 535–538.

Joyce, P.R. and Paykel, E.S. (1989) Predictors of drug response in depression. Arch. Gen. Psychiatry 46, 89–99.

Kuny, S. and Stassen, H.H. (1993) Speaking behavior and voice sound characteristics in depressive patients during recovery. J. Psychiatric Res. 27, 289–307.

Maarse, F.J., Janssen, H.J.J. and Dexel, F. (1988) A special pen for an XY-tablet. In: F.J. Maarse, J.M. Mulder, W.P.B. Sjouw and A.E. Akkerman (Eds.), Computers in Psychology: Methods, Instrumentation, and Psychodiagnostics. Swets and Zeitlinger, Amsterdam, pp. 133–139

Magill, R.A. (1993) Motor Learning: Concepts and Applications, 4th Edn. Brown and Benchmark, Madison, Indianapolis, Melbourne, Oxford, pp. 141–143.

Nilsonne, A. (1988) Speech characteristics as indicators of depressive illness. Acta Psychiatr. Scand. 77, 253–263.

Parker, G., Hadzi-Pavlovic, D., Brodaty, H., Boyce, P., Mitchell, P., Wilhelm, K., Hickie, I. and Eyers, K. (1993) Psychomotor disturbance in depression: defining the constructs. J. Affect. Disord. 27, 255–265.

Parker, G., Hadzi-Pavlovic, D., Wilhelm, K., Hickie, I., Brodaty, H., Boyce, P., Mitchell, P. and Eyers, K. (1994) Defining melancholia: properties of a refined sign-based measure. Br. J. Psychiatry 164, 316–326.

Rogers, D., Lees, A.J., Smith, E., Trimble, M. and Stern, G.M. (1987) Bradyphrenia in Parkinson's disease and psychomotor retardation in depressive illness. Brain 110, 761–776.

Sabbe, B., Hulstijn, W., Van Hoof, J.J.M. and Zitman, F.G. (1996a) Fine motor retardation and depression. J. Psychiatric Res. 30, 295–306.

Sabbe, B., Van Hoof, J.J.M., Hulstijn, W. and Zitman, F.G. (1996b) Changes in fine motor retardation in depressed patients treated with fluoxetine. J. Affect. Disord. 40, 149–157.

Sabbe, B., Hulstijn, W., Van Hoof, J.J.M., Tuynman-Qua, H.G. and Zitman, F.G. Retardation in depressed patients under treatment: Assessment of the motor component (submitted).

Stassen, H.H., Bomben, G. and Günther, E. (1991) Speech characteristics in depression. Psychopathology 24, 88–105.

Van Hoof, J.J.M., Hulstijn, W., Van Mier, J.I.A.J. and Pagen M. (1993) Fine drawing and psychomotor retardation: Preliminary results. J. Affect. Disord. 29, 263–266.

Van Mier, J.I.A.J. and Hulstijn, W. (1993). The effects of motor complexity on initiation time in writing and drawing. Acta Psychol. 84, 231–251.

Widlöcher, D. and Ghozlan, A. (1989) The measurement of retardation in depression. In: I. Hindmarch and P.D. Stonier (Eds.), Human Psychopharmacology: Measures and Methods, Vol. 2. John Wiley, New York, pp. 1–22.

Widlöcher, D. and Hardy-Bayle, M.C. (1989) Cognition and control of action in psychopathology. European Bulletin of Cognitive Psychology 12, 63–70.

Zung, W.K. (1965). A self-rating depression scale. Arch. Gen. Psychiatry 12, 63–70.