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Increase of serum creatine phosphokinase in catatonia: an investigation in 32 acute catatonic patients

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SYNOPSIS We investigated serum creatine phosphokinase (CPK) and associated parkinsonic (SEPS) and dyskinetic (AIMS) movements in 32 hospital admitted acute catatonic patients. Thirty-two ($N = 24$ without neuroleptics on admission) catatonic patients were compared with 32 non-catatonic dyskinetic psychiatric patients, 32 non-catatonic non-dyskinetic psychiatric patients and 32 healthy controls. CPK was significantly higher ($P = 0{\cdot}015$) in catatonics (mean 255·75, S.D. $\pm$226·54) than in healthy controls (38·6, $\pm$27·4) and non-catatonic non-dyskinetic psychiatric patients (57·1, $\pm$120·8) whereas there was no significant difference between catatonics and non-catatonic dyskinetic psychiatric patients (453·4, $\pm$128·5). There were significantly positive correlations between CPK and AIMS, as well as significantly negative correlations between CPK and SEPS, in all three groups. Our results suggest that increased serum CPK in catatonia may be related to occurrence of dyskinetic movements. Furthermore, we were able to distinguish a parkinsonic (low CPK, low AIMS, high SEPS) and a dyskinetic (high CPK, high AIMS, low SEPS) subtype in catatonia.

INTRODUCTION

Kahlbaum introduced the term catatonia to describe patients with a wide range of motor abnormalities including akinesia, posturing, catalepsy, rigidity, negativism, grimacing, waxy flexibility, and verbigerations (Kahlbaum, 1874). In contrast to Kahlbaum, who considered catatonia as a separate disease entity, Kraepelin (1905) and Bleuler (1911) primarily referred to catatonia as a subtype of schizophrenia and, until now, DSM-III-R (APA, 1987) has continued with this definition. However, the more recent literature has emphasized the notion that catatonia represents a syndrome rather than a separate disease entity (Gelenberg, 1976; Editorial, 1986; Fink *et al.* 1993). As such, catatonia may occur in a variety of different diseases, both organic and non-organic (Cummings, 1985; Taylor, 1990). In this context, several reports suggest a dramatic therapeutic response of catatonic syndrome to lorazepam, in so much as it can be regarded as a standard treatment (Rosebush *et al.* 1990; Menza *et al.* 1991; Rosebush & Furlong, 1991; Fink *et al.* 1993; Northoff, 1995).

Until now the pathophysiology of catatonia has remained unknown, and it has never been clarified whether catatonia has to be considered either as a primary motor disturbance (Taylor, 1990; Fink *et al.* 1993), or as a disorder of volition (Kraepelin, 1905; Mortimer *et al.* 1990; McKenna *et al.* 1991). In order to investigate motor and muscle function in catatonia we measured creatine phosphokinase (CPK) and its muscle fraction (CK-MM), which indicates cellular damage in the skeletal muscles (El-Mallakh *et al.* 1992), as well as associated parkinsonic (SEPS) and dyskinetic (AIMS) movements in 32 acute catatonic patients. Thereby, we compared catatonic patients with 32 non-catatonic dyskinetic psychiatric patients, 32 non-catatonic non-dyskinetic psychiatric patients and 32 healthy controls.

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METHOD

Subject selection

We studied 32 catatonic patients who were admitted to hospital in an acute catatonic state (acutely admitted) (16 women, 16 men; mean age, 33·4 years S.D. ± 10·8), who were selected from all of the patients admitted to our hospital between January 1990 and May 1993 (incidence, 2·8%). Twenty-four were untreated (at least 6 months off neuroleptics prior to admission, 21 never received any neuroleptics and three patients were treated with haloperidol (2–18 mg for an average duration of 2·1 ± 1·2 years) and eight had received neuroleptics, e.g. haloperidol (duration, 3·2 ± 1·1 years; dose range, 2–20 mg) either on the day of admission or in the 6 months before admission.

Catatonic syndrome was diagnosed according to criteria by Lohr & Wisniewski (1987; three from 11 symptoms) and Rosebush *et al.* (1990; four from 12 symptoms in orientation on Kahlbaum), which uses a rather strict definition of catatonia by relying on a cluster of symptoms as recommended by Gelenberg (1977). All patients had to be classified as catatonic, according to both of these criteria lists, by two independent psychiatrists (G.N., J.W.) with special experience in catatonia. Co-morbid diagnosis according to DSM-III-R (APA, 1987) were made on discharge by two independent psychiatrists with a structured clinical interview.

Moreover, we investigated 32 acutely admitted ($N = 15$) or chronically hospitalized ($N = 17$) non-catatonic and dyskinetic (dyskinesia was defined by AIMS: day 0, 21·5 ± 8·2) treated (average duration of neuroleptic (i.e. haloperidol, 2–25 mg) treatment was 8·6 ± 4·5 years) psychiatric patients (diagnosis according to DSM-III-R for 28 patients was 295.6 and for four patients, 295.3), matched with regard to age and sex (mean age, 33·8 ± 11·2) to our catatonic patients. In addition, we investigated 32 acutely admitted non-catatonic and non-dyskinetic partially untreated (23 never received any neuroleptics or antidepressants whereas nine patients were treated with neuroleptics (i.e. haloperidol 2–19 mg) for an average duration of 2·3 ± 1·2 years) psychiatric patients (diagnosis according to DSM-III-R; was: 10 patients, 295.3; 10 patients, 295.6; six patients, 296.3; six patients, 296.6), matched with regard to age and sex (mean age, 33·9 ± 11·1; 16 women, 16 men) to our catatonic patients. Thirty-two healthy controls, medical students and colleagues who were matched to catatonic patients (mean age, 33·9 ± 10·9; 16 women, 16 men), were also investigated. These healthy controls were different from those who were used for the study of laboratory error.

Patients ($N = 11$) with concomittant Parkinson's disease or neuroleptic malignant syndrome (NMS) were excluded. All patients and controls in our study samples were white and of Caucasian race.

General psychopathology

General psychopathology was evaluated by Global Assessment Scale (GAS; Endicott *et al.* 1976) and Brief Psychiatric Rating Scale (BPRS; Overall & Gorman, 1962).

Movements

Parkinsonic movements were evaluated by the scale for the assessment of extrapyramidal side effects (SEPS; Simpson & Angus, 1970) and dyskinetic movements were evaluated by Abnormal Involuntary Movement Scale (AIMS; Guy, 1976).

All psychopathological ratings were performed independently by G.N. and J.W., whose intra-rater and inter-rater reliability revealed average intraclass correlations coefficients between 0·90 and 0·95.

Study design

After inclusion into our study sample all catatonic patients received daily, lorazepam 2–4 × 1 mg (mean, 3·3 mg), either orally ($N = 10$) or intravenously ($N = 22$). All above mentioned psychopathological ratings and evaluations were performed on day 0 before initial medication with lorazepam. According to their response to lorazepam we distinguished responders and non-responders among catatonic patients: drug response to lorazepam was defined by resolution of the catatonic syndrome on day 1 (24 h after admission), so that the patients could no longer be classified as catatonic according to the criteria by Lohr & Wisniewski and Rosebush *et al.* (see above). Non-responders, with regard to lorazepam, were defined by non-resolution of catatonic syndrome

Table 1. *Serum, CPK, AIMS and SEPS in catatonia and non-catatonic psychiatric patients*

		Serum-CPK U/l		AIMS		SEPS	
	N	Day 0 Mean (±S.D.)	Day 21 Mean (±S.D.)	Day 0 Mean (±S.D.)	Day 21 Mean (±S.D.)	Day 0 Mean (±S.D.)	Day 21 Mean (±S.D.)
All catatonics	32	255·75 (226·5)	30·8 (30·6)	15·2 (11·8)	2·7 (3·3)	18·2 (7·1)	13·8 (7·4)
Untreated	24	304·9 (228·1)	32·6 (34·3)	17·0 (12·3)	3·2 (3·4)	17·4 (7·6)	14·2 (7·6)
Treated	8	108·3 (152·4)	26·3 (15·8)	9·6 (8·6)	1·4 (2·5)	20·5 (5·4)	12·5 (7·1)
Non-affective	21	290·6 (219·4)	27·3 (31·1)	17·3 (11·9)	2·5 (3·3)	17·5 (7·6)	14·1 (8·1)
Affective	11	189·2 (235·3)	38·1 (29·7)	11·1 (10·6)	3·3 (3·5)	19·5 (6·4)	13·5 (6·4)
Non-schizophrenic	15	184·3 (236·3)	31·4 (27·2)	11·2 (11·5)	2·6 (3·2)	20·6 (6·1)	15·8 (7·2)
Schizophrenic	17	318·7 (203·9)	30·6 (34·1)	18·6 (11·2)	2·9 (3·5)	16·1 (7·6)	12·2 (7·4)
Non-residual-schizo.	23	303·7 (220·8)	35 (34·7)	17·2 (12·3)	3·2 (3·5)	17·2 (7·7)	14·9 (7·6)
Residual-schizo.	9	133·4 (203·3)	20·8 (11·6)	9·9 (8·7)	1·7 (2·5)	20·7 (5·1)	11 (6·4)
Non-responder	15	68·1 (119·6)	23·3 (13·8)	5·2 (6·1)	1·9 (2·9)	21·3 (6·8)	12·9 (8·2)
Responder	17	421·3 (157·5)	37·7 (39·2)	23·9 (7·8)	3·4 (3·5)	15·4 (6·5)	14·7 (6·7)
Non-catatonic dyskinetic	32	453·4 (128·5)	298·8 (152·6)	21·5 (8·2)	17·6 (7·1)	13·4 (6·4)	13·5 (5·9)
Non-catatonic non-dyskinetic	32	57·1 (120·8)	48·2 (98·5)	0·3 (0·1)	0·4 (0·1)	6·5 (5·8)	12·5 (7·8)

on day 1 (24 h after admission). Hence non-response was defined only as non-response on day 1 but not as general non-response to lorazepam.

Over the next 3 weeks, medication with lorazepam was continued (2–4 mg/day). In addition, depending on co-morbid diagnosis, 24 patients received neuroleptics (haloperidol, benperidol; 12 responders, 12 non-responders), six patients received tricyclic antidepressants (three responders, two non-responders), six patients received lithium (three responders, three non-responders), and two received exclusively lorazepam (two non-responders, who both underwent treatment with ECT). Depending on their diagnosis non-catatonic dyskinetic and non-catatonic non-dyskinetic psychiatric patients were treated with either antidepressants (doxepin, 25–175 mg) or neuroleptics (haloperidol, 2–25 mg). As in catatonic patients psychopathological ratings were performed on these patients on day 0, before initial medication.

On day 21 (which was chosen arbitrarily), all psychopathological ratings and evaluation of catatonic syndrome were repeated.

CPK determination

Serum samples for CPK analysis were obtained from all patients at 8.00 a.m., if possible. We tried to account for influencing factors (Meltzer, 1976) e.g. intramuscular injections (no injections for 3 months before admission), alcoholism, muscle trauma, physical activity (abnormal high physical activity due to sports, restlessness, akathisia, agitation, etc.) and sleep deprivation by excluding patients with these features ($N = 18$) from our study samples.

Serum CPK-concentrations as well as the three subunits (MM, MB, BB) were determined by Rosalki's method using a commercially available enzyme kit (Rosalki, 1967). Average values (upper limit of normal CPK activity is 50 mouse units (MU)/ml for white women and 70 MU/ml for white men) in our laboratory are similar to the values found in Meltzer's studies (Meltzer, 1973). The average laboratory error on paired samples drawn from 20 healthy controls in our hospital staff is 2% (coefficient of variation of samples). These controls were different from the ones used for our study as control group.

Statistical analysis

All results were expressed as means and standard deviations. The three main groups, all catatonics, non-catatonic dyskinetic and non-catatonic non-dyskinetic psychiatric patients, were statistically compared by one-way ANOVA, differences between single groups were tested by Scheffé's test. The effect of investigated variables (CPK, AIMS, SEPS) in responders/non-responders and treated/untreated catatonics as well as in diagnostic subgroups (see Table 1) among the 32 catatonic patients were tested by Multivariante Repeated Measurements ANOVA (MANOVA). Moreover, we conducted three repeated meas-

urement ANOVAs for each of the three variables (CPK, AIMS, SEPS). Correlations among the three variables (CPK, AIMS, SEPS) were assessed using Pearson's product moment correlation coefficients. All computations were executed with the SPSS-X statistics software system (SPSS-X Statistic System, 1991).

RESULTS

Catatonic patients

According to Rosebush *et al.* (1990) on day 0, 62% of all catatonic patients showed immobility, 71% staring, 80% mutism, 54% autism, 60% posturing, 43% rigidity, 39% negativisms, 92% catalepsy, 42% grimacing, 30% echolalia, 45% stereotypies and 38% verbigerations. On day 0, there were no significant differences between responders and non-responders with regard to each of the 12 catatonic symptoms. No significant correlations between particular catatonic symptoms and CPK, AIMS, and SEPS could be found.

Co-morbid diagnosis

Diagnosis according to DSM-III-R included the following diagnosis among the 32 catatonic patients:

Residual schizophrenia (295.6), $N = 9$;
Catatonic schizophrenia (295.2), $N = 7$;
Paranoid schizophrenia (295.3), $N = 1$;
Major depression (296.3), $N = 5$;
Bipolar disorder (296.6), $N = 6$;
Brief reactive psychosis (298.8), $N = 2$.

In addition, we had two catatonic patients with organic diseases (renal encephalopathy, hypoxic brain disease).

Response to lorazepam

Seventeen patients (10 of them received lorazepam orally and seven intravenously) showed a dramatic response to lorazepam, so that they were no longer classified as catatonic on day 1 (i.e. 24 h after admission). Fifteen patients were still diagnosed as catatonic on day 1 according to the criteria of Lohr & Wisniewski and Rosebush *et al.* As mentioned previously eight patients received neuroleptics either on the day of admission or in the 6 months prior to admission. After 24 h, five of these patients were evaluated as non-responders and three as responders. On day 21, five patients from the 15 non-responders were still classified as catatonic according to the criteria of Lohr & Wisniewski and Rosebush *et al.* (all of the patients received ECT which relieved their catatonia). None of the responders was evaluated as a catatonic on day 21.

There were no significant differences (χ^2-test) with regard to age and sex between responders (mean age, $34{\cdot}9 \pm 12{\cdot}3$; sex, eight women, nine men) and non-responders (mean age, $31{\cdot}9 \pm 12{\cdot}0$; sex, eight women, seven men).

General psychopathology

In all catatonic patients the mean GAS-score was $10{\cdot}3 \pm 4{\cdot}9$ and mean BPRS-score was $60{\cdot}2 \pm 15{\cdot}2$ on the day of admission before initial medication. On day 0 there were no significant differences between responders and non-responders, as well as between the other catatonic subgroups. Differences between day 0 (see above) and day 21 (GAS, mean $72{\cdot}4 \pm 15{\cdot}6$; BPRS, mean $17{\cdot}7 \pm 25{\cdot}4$) were significant (GAS, $P = 0{\cdot}004$; BPRS, $P = 0{\cdot}0025$).

For non-catatonic dyskinetic psychiatric patients the mean GAS-score was $13{\cdot}4 \pm 5{\cdot}6$ and the mean BPRS-score was $59{\cdot}7 \pm 16{\cdot}3$. For non-catatonic non-dyskinetic psychiatric patients the mean GAS-score was $15{\cdot}6 \pm 4{\cdot}8$ and the mean BPRS-score was $55{\cdot}9 \pm 14{\cdot}8$.

Movements

AIMS-scores (see Table 1) between catatonic-responders and non-catatonic dyskinetic psychiatric patients did not differ significantly on day 0, whereas on day 21 they differed significantly ($P < 0{\cdot}001$). Catatonic-responders and non-catatonic non-dyskinetic psychiatric patients differed significantly ($P < 0{\cdot}001$) in their AIMS-scores on day 0.

No significant correlations between GAS, BPRS on the one hand and AIMS, SEPS, CPK on the other hand either on day 0 or on day 21 could be obtained in all three groups (catatonic, non-catatonic dyskinetic, non-catatonic non-dyskinetic).

Serum CPK and movements

Results for CPK in all groups and subgroups can be seen in Table 1. Nine catatonic patients had CPK-values within the normal range whereas all other catatonics had increased serum CPK. Elevation of serum CPK was due to the

Table 2. *Correlations between CPK, AIMS and SEPS in catatonic and non-catatonic psychiatric patients*

		CPK-AIMS				CPK-SEPS				SEPS-AIMS			
		Day 0		Day 21		Day 0		Day 21		Day 0		Day 21	
	N	*r*	*P*	*r*	*P*	*r*	*P*	*r*	*P*	*r*	*P*	*r*	*P*
All catatonics	32	0·82	0·0001	0·043	NS	0·63	0·0001	0·073	NS	0·42	0·016	0·046	NS
Untreated	24	0·84	0·0001	0·13	NS	0·61	0·0001	0·12	NS	0·39	0·05	0·67	NS
Treated	8	0·70	0·05	0·57	NS	0·61	NS	0·47	NS	0·36	NS	0·2	NS
Non-affective	21	0·87	0·0001	0·009	NS	0·67	0·0009	0·63	NS	0·36	NS	0·22	NS
Affective	11	0·77	0·014	0·20	NS	0·53	0·086	0·35	NS	0·50	NS	0·35	NS
Non-schizophrenic	15	0·85	0·0004	0·18	NS	0·87	0·002	0·14	NS	0·64	0·01	0·194	NS
Schizophrenic	17	0·76	0·0032	0·05	NS	0·37	NS	0·026	NS	0·194	NS	0·04	NS
Non-chronic-schizo.	23	0·83	0·0001	0·17	NS	0·68	0·0002	0·015	NS	0·41	0·049	0·035	NS
Chronic-schizo.	9	0·72	0·027	0·82	0·005	0·267	NS	0·11	NS	0·20	NS	0·2	NS
Non-responder	15	0·82	0·0004	0·43	NS	0·77	0·0006	0·25	NS	0·59	0·018	0·22	NS
Responder	15	0·39	NS	0·25	NS	0·4	NS	0·01	NS	0·14	NS	0·16	NS
Non-catatonic dyskinetic	32	0·81	0·001	0·48	NS	0·64	0·01	0·67	NS	0·77	0·001	0·18	NS
Non-catatonic non-dyskinetic	32	0·71	0·034	0·58	NS	0·39	0·05	0·37	NS	0·64	0·01	0·56	NS

subunit MM meanwhile the other subunits of CPK (MB, BB) were not increased. Moreover, for all catatonic patients, there was a significant correlation ($r = 0{\cdot}64$, $P = 0{\cdot}01$) between duration of catatonia (mean $6{\cdot}5 \pm 5{\cdot}9$ days) and increase of CPK.

On day 0 there were significant differences for CPK (see Table 1) between catatonic patients and non-catatonic dyskinetic psychiatric patients ($P = 0{\cdot}048$) as well as between catatonic patients and non-catatonic non-dyskinetic psychiatric patients ($P = 0{\cdot}028$). There were no significant differences for CPK on day 0 between catatonic-responders and non-catatonic dyskinetic psychiatric patients as well as between catatonic-non-responders and non-catatonic non-dyskinetic psychiatric patients. On day 21 (see Table 1) CPK was significantly higher (CPK, $P = 0{\cdot}013$) in non-catatonic dyskinetic psychiatric patients than in catatonic patients, whereas CPK did not differ significantly between catatonic patients and non-catatonic non-dyskinetic psychiatric patients. All three groups (catatonic, non-catatonic dyskinetic, non-catatonic non-dyskinetic) showed significantly positive correlations between CPK and AIMS as well as significantly negative correlations between CPK and SEPS (see Table 2). There were no significant differences in CPK, AIMS and SEPS between patients with affective and schizophrenic psychosis among non-catatonic non-dyskinetic psychiatric patients.

In controls the mean CPK was $38{\cdot}6 \pm 27{\cdot}4$, which differed significantly form catatonic patients ($P = 0{\cdot}015$) as well as from non-catatonic dyskinetic psychiatric patients ($P < 0{\cdot}001$) on day 0. Within the control group males ($N = 16$) the mean was $41{\cdot}2 \pm 29{\cdot}4$ and for the control group females ($N = 16$) the mean was $36{\cdot}0 \pm 25{\cdot}8$. In our catatonic patients, as well as in the two other groups (non-catatonic dyskinetic, non-catatonic non-dyskinetic), there were no significant differences between males and females for CPK, AIMS and SEPS.

Catatonic subgroups

Results from CPK, AIMS, and SEPS in all catatonic patients as well as in the different subgroups can be seen in Table 1. MANOVA for all three variables (CPK, AIMS, SEPS) in all catatonic subgroups showed that only responders/non-responders had an significant effect ($P < 0{\cdot}001$), whereas all other catatonic subgroups (untreated/treated, non-affective/affective, non-schizophrenic/schizophrenic, non-residual schizophrenia/residual schizophrenia) remained without significant effect. The distinction between responders and non-responders was significantly influenced by day 0/21 ($P < 0{\cdot}001$) but not by treatment/non-treatment or diagnosis. Distinction of responders and non-responders is further supported by a Repeated Measurement ANOVA for each of the three variables (CPK, AIMS, SEPS): responders and

non-responders could be distinguished significantly with regard to CPK ($P < 0.001$) on day 0 (effect of day; $P < 0.001$) and AIMS ($P < 0.001$) on day 0 (effect of day; $P < 0.001$).

There was no significant effect of responders/non-responders on SEPS, except that day 0 had a significant effect ($P = 0.009$). Treatment or non-treatment in responders and non-responders had no significant influence on CPK, AIMS and SEPS.

DISCUSSION

We found significantly higher serum CPK in catatonic patients than in non-catatonic non-dyskinetic psychiatric patients and healthy controls. Systematic investigations of serum CPK in catatonia have not been reported yet. One case report, suffering from lethal catatonia, showed an increased serum CPK (227) (Häfner & Kasper, 1982). Other reports concerning lethal catatonia either found normal CPK or did not mention serum CPK in their criteria of laboratory abnormalities (Stauder, 1934; Mann *et al.* 1986; Hermle & Oepen, 1986; Ainsworth, 1987; Castillo *et al.* 1989; Fleischacker *et al.* 1990).

A similar increase of serum CPK has also been reported in patients with acute schizophrenia and acute affective disorder: these patients showed brief duration of increase of CPK, whereas patients with residual schizophrenia showed less increase of CPK (Meltzer, 1976). In catatonia too, we found elevation of CPK only on day 0 but no longer on day 21. Moreover, catatonic patients with a co-morbid diagnosis of residual schizophrenia showed lower CPK than non-residual schizophrenic catatonics (see Table 1). Elevations of serum CPK in our acute catatonic patients (see Table 1) were not as high as in neuroleptic malignant syndrome (NMS), where increases of a great magnitude (82% of all patients > 300, often > 1000) can often be observed (Caroff, 1980; Levenson, 1985; Addonizio *et al.* 1987; Fleischacker *et al.* 1990; Sczesni *et al.* 1991). Therefore, unlike in NMS, the diagnostic value of CPK in catatonia seems to be questionable. Nevertheless, the explanation for such a moderate increase of serum CPK in catatonic patients remains open.

We found significantly positive correlations between increase of serum CPK and occurrence of dyskinetic movements, measured by AIMS, as well as significantly negative correlations between CPK and parkinsonic movements, measured by SEPS (see Table 2). Meltzer too found a correlation between motor activity and serum CPK in patients with schizophrenia and depression (Meltzer, 1975). Hence dyskinetic movements with their increased motor activity may have caused the increase of serum CPK in our catatonic patients. Such a conclusion is supported by the fact that on day 0 CPK was found in non-catatonic dyskinetic psychiatric patients to be as high as in catatonic-responders, both showing no significant differences in their AIMS-scores. Whereas, CPK on day 0 did not differ significantly between catatonic non-responders with their low AIMS-scores (see Table 1) and non-catatonic non-dyskinetic psychiatric patients.

Considering methodological shortcomings such as, no exact determination of motor activity before admission in newly admitted patients and no determination of CPK on day 1, such a conclusion has to be considered cautiously. Other studies showed that hyperkinetic movements *per se* may not cause increase of CPK (Goode & Meltzer, 1976). Nevertheless, significant positive correlations between AIMS and CPK on day 0 as well as distinction between responders and non-responders in catatonia with regard to CPK and AIMS (see below) suggest that increase of CPK in our catatonic patients may somehow be related with occurrence of dyskinesias.

Furthermore, we were able to distinguish responders and non-responders in catatonia with regard to CPK, parkinsonic and dyskinetic movements: patients with a good response to lorazepam showed significantly higher CPK and significantly more dyskinetic movements (AIMS) than non-responders who showed higher SEPS-scores on day 0 (see above). Hence, with regard to movements, responders may be characterized as a dyskinetic subtype, whereas non-responders may, rather, be called a parkinsonian subtype. Such a distinction between a dyskinetic and a parkinsonian subtype in catatonia is supported by studies in schizophrenia, which distinguished such subtypes on the basis of their association with positive and negative symptoms. (Mortimer *et al.* 1990; McKenna *et al.* 1991). Pathophysiologically,

such catatonic subtypes may represent different functional deregulations of different transmitter systems (GABA-ergic projections in dyskinetic subtype with its good response to lorazepam (Rosebush *et al.* 1992); dopaminergic balance in parkinsonic subtype with its non-response to lorazepam) within the cortico–striatal–thalamo–cortical circuit (Northoff, 1995), known as the 'motor loop' (Alexander *et al.* 1990).

REFERENCES

Addonizio, G., Susman, V. L. & Roth, S. D. (1987). Neuroleptic malignant syndrome: review and analysis of 115 cases. *Biological Psychiatry* **22**, 1004–1020.

Ainsworth, P. (1987). A case of lethal catatonia in a 14 year old girl. *British Journal of Psychiatry* **150**, 110–112.

Alexander, G. E., Cratcher, M. D. & DeLong, M. R. (1990). Basal ganglia thalamo cortical circuits. *Progress in Brain Research* **9**, 1–50.

American Psychiatric Association (1987). Commitee on nomenclature and statistics, *Manual of Mental Disorders, 3rd edn.* APA: Washington, DC.

Bleuler, E. (1911). *Dementia praecox oder die Gruppe der Schizophrenien*. Deutricke: Wien.

Caroff, S. T. (1980). The neuroleptic malignant syndrome. *Journal of Clinical Psychiatry* **41**, 79–83.

Castillo, E., Rubin, R. T. & Hoelsboer-Traechsler, E. (1989). Clinical differentiation between lethal catatonia and neuroleptic malignant syndrome. *American Journal of Psychiatry* **146**, 324–328.

Cummings, J. L. (1985). *Clinical Neuropsychiatry*. Stratton: New York.

Editorial (1986). Catatonia. *Lancet* ii, 954–956.

El-Mallakh, R. S., Egan, M. & Wyatt, R. J. (1992). Creatine kinase and enolase: intracellular enzymes serving as markers of central nervous system damage in neuropsychiatric disorders. *Psychiatry* **55**, 392–402.

Endicott, J., Spitzer, R., Flies, J., Schwartz, U. & Fink, U. (1976). The Global Assessment Scale. *Archives of General Psychiatry* **33**, 766–771.

Fink, M., Bush, G. & Francis, A. (1993). Catatonia: a treatable disorder occasionally recognized. *Directions in Psychiatry* **13**, 1–7.

Fleischhacker, W., Unterweger, B., Kane, J. M. & Hinterhuber, H. (1990). The neuroleptic malignant syndrome and its differentiation from lethal catatonia. *Acta Psychiatrica Scandinavica* **81**, 3–5.

Gelenberg, A. J. (1976). The catatonic syndrome. *Lancet* i, 1339–1341.

Gelenberg, A. J. (1977). Criteria for the diagnosis of catatonia. *American Journal of Psychiatry* **134**, 462–463.

Goode, D. J. & Meltzer, H. J. (1976). Effects of isometric exercise on serum creatine phosphokinase activity. *Archives of General Psychiatry* **33**, 1207–1211.

Guy, W. (1976). *Assessment Manual for Psychopharmacology. DHEW 76-338*, NIH, Psychopharmacology Research: Rockville, TS.

Häfner, H. & Kasper, S. (1982). Akute lebensbedrohliche Katatonie. *Nervenarzt* **53**, 385–394.

Hermle, L. & Oepen, G. (1986). Zur Differentialdiagnose der akut lebensbedrohlichen Katatonie und des malignen Neuroleptik-asyndromsein kasuistischer Beitrag. *Fortschritte der Neurologie und Psychiatrie* **54**, 189–195.

Kahlbaum, K. L. (1874). *Die Katatonie*. Hirschwald: Berlin.

Kraepelin, E. (1905). *Lehrbuch der Psychiatrie*. Barth: München.

Levenson, J. L. (1985). Neuroleptic malignant syndrome. *American Journal of Psychiatry* **142**, 1137–1145.

Lohr, J. & Wisniewski, A. (1987). *Movement Disorders*. Wiley: Chichester.

McKenna, P., Lund, C., Mortimer, A. & Biggins, C. (1991). Motor, volitional, and behavioural disorders in schizophrenia. *British Journal of Psychiatry* **158**, 323–336.

Mann, S. C., Caroff, S. N., Bleier, H. R., Welz, W., Kling, M. & Hayashida, M. (1986). Lethal catatonia. *American Journal of Psychiatry* **143**, 1374–1381.

Meltzer, H. Y. (1973). Creatine phosphokinase activity and clinical symptomatology. *Archives of General Psychiatry* **29**, 589–593.

Meltzer, H. Y. (1975). Neuromuscular abnormalities in the major mental illnesses. In *Biology of the Major Psychoses* (ed. D. X. Freedman), pp. 54–72. Blackwell: New York.

Meltzer, H. Y. (1976). Serum creatine phosphokinase in schizophrenia. *American Journal of Psychiatry* **133**, 192–197.

Menza, M. (1991). Lorazepam and catatonia. *Journal of Clinical Psychiatry* **52**, 186–187.

Mortimer, A. M., Lund, C. & McKenna, P. (1990). The positive–negative dichotomy in schizophrenia. *British Journal of Psychiatry* **157**, 41–49.

Northoff, G. (1995). Effects of benzodiazepines in catatonia – a pathophysiological model. In *Endogenous Psychosis* (ed. H. Beckmann and K. J. Neumärker), pp. 145–159. Ullstein Mosby: New York.

Overall, J. E. & Gorham, D. R. (1962). The Brief Psychiatric Rating Scale. *Psychological Reports* **10**, 799–812.

Rosalki, S. E. (1967). An improved procedure for serum creatine phosphokinase determination. *Journal of Laboratory Clinical Medicine* **69**, 696–705.

Rosebush, P. & Furlong, M. (1991). A consideration of the mechanisms by which lorazepam might treat catatonia. *Journal of Clinical Psychiatry* **52**, 187–188.

Rosebush, P., Furlong, B. & Mazurek, M. (1990). Catatonic syndrome in a general psychiatric inpatient population: frequency, clinical presentation, and response to lorazepam. *Journal of Clinical Psychiatry* **51**, 357–362.

Rosebush, P., Furlong, B. & Mazurek, M. (1992). The treatment of catatonia: benzodiazepines or ECT? *American Journal of Psychiatry* **149**, 9–10.

Sczesni, B., Schröder, J., Becker, H. & Przuntek, H. (1991). Das neuroleptische maligne Syndrom. *Wiener Klinische Wochenschrift* **103**, 1–7.

Simpson, G. M. & Angus, J. W. S. (1970). A rating scale for extrapyramidal side effects. *Acta Psychiatrica Scandinavica* (Suppl.) **212**, 11–19.

Stauder, K. H. (1934). Die tödliche Katatonie. *Archiv für Psychiatrie* **102**, 614–634.

Taylor, M. (1990). Catatonia: a review of the behavioral neurologic syndrome. *Neuropsychiatry, Neuropsychology and Behavioral Neurology* **3**, 48–72.