Table 1. Serum Hormonal Levels

Hormones		Case 1 (female)	Case 2 (male)
Prolactin	Observed	169 ng/mL	6.6 ng/mL
	Normal	2–20 ng/mL	2.1–17.7 ng/mL
Estradiol	Observed	73 pg/mL	NA
	Normal	50–150 pg/mL	
FSH	Observed	<1.0 MIU/mL	4.4 MIU/mL
	Normal	1–7.5 MIU/mL	1–15 MIU/mL
LH	Observed	<1.0 MIU/mL	8.2 MIU/mL
	Normal	1–27 MIU/mL	1.3–12 MIU/mL
Testosterone	Observed	NA	798 ng/dL
	Normal		20–990 ng/dL

FSH, follicle stimulating hormone; LH, luteinizing hormone.

Table 2. Bone Mineral Densities Measured by DEXA

Cases	Site	BMD g/cm^2	Compared to PBM		Age-matched	
			SD	% BMD	SD	% BMD
Case 1	Femoral neck	0.675	−2.20	75%	−2.02	77%
	Hip total (left)	0.710	−2.21	73%	−2.18	73%
	Ward's triangle	0.512	−2.58	64%	−2.06	69%
	L1–L4	1.032	−0.14	99%	−0.11	99%
Case 2	Femoral neck	0.717	−2.38	73%	−0.96	87%
	Hip total (left)	0.886	−1.43	83%	−0.62	92%
	Ward's triangle	0.544	−2.40	65%	−0.46	91%
	L1–L4	0.925	−1.51	85%	−0.99	90%

BMD, bone mineral density; PBM: peak bone mass.

(Alder et al 1985). Both patients were heavy smokers, and tobacco smoking has been shown to interfere with the protective action of estrogens on bone mineralization. Pocock et al (1989) showed this difference in the lumbar spine and proximal femur bone densities in identical twins discordant for smoking. Polydipsia is another potential risk factor for osteoporosis, since the resulting secondary polyuria may cause excess loss of urinary calcium. Delva et al (1989) have demonstrated reduced BMD in 10 young male schizophrenic patients with polydipsia. If the prevalence and severity of osteoporosis is elevated among persons with chronic schizophrenia, then it represents a medical condition that should receive additional attention.

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Neuroleptic Malignant Syndrome and Catatonia: One Entity or Two?

To the Editor.

Fink discusses the relationship between neuroleptic malignant syndrome (NMS) and catatonia and argues that both are "variants of the same disorder" (Fink 1996). Due to the fact that pathophysiology of catatonia remains largely unknown, such comparisons are very useful for elucidation of pathophysiological hypothesis. Nevertheless, besides their similarities there are also several dissimilarities between NMS and catatonia that would contradict Fink's hypothesis of a common disorder. I would like to point out some of these differences between NMS and catatonia, particularly the distinction between the clinical–phenomenological (a) and the neuropathological (b) level.

As to (a): NMS and catatonia show both akinesia such that it may be difficult to distinguish them clinically with regard to hypokinesias. But while catatonic patients often do show behavioral abnormalities such as automatisms, negativisms, etc. as well as hyperkinesias (stereotypies, etc.), patients with NMS only show hypokinesias. Even hypokinetic symptoms differ because catatonic patients show posturing and flexibilitas cerea ("smooth rigidity"), whereas NMS patients show the typical parkinsonian kind of rigidity with the cog–wheel phenomenon and no posturing at all. Thus from the purely motor point of view catatonia and NMS not only show similarities but, in addition, several differences as well. Phenomenologically, with regard to subjective experience, catatonic patients retrospectively report either intense and uncontrollable anxieties or unresolvable ambivalences in their cognitions (Northoff et al 1996a). In contrast to patients with Parkinson's disease, catatonic patients often do not realize that their movements are functionally altered; i.e., they are not aware of their hypo- and/or hyperkinesias (Northoff et al 1996b). Clinical experience shows that patients with neuroleptic-induced movements disorders do fully realize their motor alterations such that, with regard to subjective experience, NMS can rather be compared with Parkinson's disease and neuroleptic-induced extrapyramidal side effects than with catatonia.

As to (b): Akinesia in Parkinson's disease is related with hypofunction of striatal dopamine due to nigrostriatal dopami-

nergic deficiency. Similar to Parkinson's disease, NMS may probably be due to striatal dopaminergic hypofunction caused by blockade of striatal dopamine receptors (Jauß et al 1994). Such functional similarities may account for a symptomatological resemblence between Parkinson's disease and NMS both showing cog–wheel rigidity and akinetic crisis. In contrast to NMS, there are at present no indications for primary striatal dopaminergic dysfunction in catatonia: Findings of elevated plasma HVA may be rather related with mesolimbic and mesocortical dopaminergic pathways than with nigrostriatal dopamine, which would explain the often observed association of catatonia with schizophrenia (Northoff et al 1996c). In catatonia, higher cortical centers such as the supplementary motor area (SMA), the anterior cingulum, and the dorsolateral prefrontal cortex (DLPFC) may rather be primarily altered: Similiar to Parkinson's disease, catatonic patients, as demonstrated in ball experiments, show a deficit of the internal initation of movements (Northoff et al 1995a) closely related with internal initation of movements (Jahanshahi et al 1995) so that one would expect hypofunction of SMA in catatonia. Preliminary results of motor activation studies in functional MRT with postacute catatonic patients would support such a hypothesis showing hypoactivation of SMA while motor cortex activation did not differ from healthy controls (Northoff et al 1995b). Furthermore, following the subjective experiences in catatonic patients (see above), one would expect that regions such as the anterior cingulum and/or the DLPFC, where emotions and/or cognitions become transformed into movements, may be functionally altered in catatonia.

Conclusions: Clinically, phenomenologically and neuropathologically NMS and catatonia show similarities as well as differences. Especially with regard to hypokinesias, there seems to be an important symptomatological overlap between NMS and catatonia whereas only the latter shows behavioral abnormalities and hyperkinesias. Thus clinically and phenomenologically NMS rather seems to resemble Parkinson's disease than catatonia. Therefore it can be hypothesized that NMS may be similiar to Parkinson's disease, related to primary striatal dopaminergic dysfunction. In contrast, catatonia may be primarily caused by cortical, i.e., frontal dysfunction, as it is assumed by Taylor (1990). Such a frontal dysfunction would explain behavioral abnormalities as well as subjective experiences and it may lead to secondary down-regulation of striatal dopaminergic function causing hypokinesias more or less similar to NMS and Parkinson's disease. Hence NMS and catatonia should be regarded as two distinct disorders; i.e., as striatal and as frontal; with partial pathophysiological overlappings, concerning regulation of striatal dopaminergic function, than "variants of the same disorder" (Fink 1996).

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Response

To the Editor.

Dr. Northoff faults our suggestion that the neuroleptic malignant syndrome (NMS) be viewed as a variant of catatonia and not as a distinct dopaminergic overdrive syndrome (Fink 1996). He finds these syndromes distinct in clinical phenomenology and theoretic neuropathology.

He asserts that motor rigidity is only one of a range of motor signs in catatonia while it is the single most prominent motor sign in NMS. While that observation is essentially correct, such a limitation is not sufficient to demarcate two conditions. We consider dementia, delirium, paranoia, and mania as variants of one condition in neurosyphilis when that etiology is defined. And we are not fazed by patients with bipolar affective disorders who appear depressed at one time, manic on another, once delusional, and on another occasion, melancholic. In like fashion, I suggest that NMS is a variant of catatonia because the variants may be seen in the same subjects (White 1991, 1992), they respond to the same interventions, and in many instances the manifestations are often indistinguishable.

Dr. Northoff compares the motor rigidity of NMS to that seen in parkinsonism, emphasizing the cog–wheel phenomenon and an absence of posturing presumably seen in both conditions. He is correct in this suggestion, that cases of NMS appear to have

motor signs that could be assessed as parkinsonism, but such a similarity is limited to appearance only. The age of incidence, slow almost imperceptible onset, and absence of fever and vegetative signs separate Parkinson cases from those of NMS where onset is sudden, most often in young adults, with fever and autonomic instability essential to the diagnosis. It is unclear how associating these syndromes is either clinically or theoretically helpful.

He has assessed the subjective experience of patients with NMS and with catatonia, finding that those afflicted with catatonia report intense and uncontrollable anxieties and unresolvable ambivalence, while those with NMS (and parkinsonism) do not realize that their movements are functionally altered (Northoff et al 1996). As he cites his own data in press for these observations, I am unable to assess this interesting argument, and look forward to confirmatory studies.

Dr. Northoff speculates that the akinesia of parkinsonism is related to nigrostriatal dopaminergic deficiency, and believes that the same pathophysiology is a feature of NMS, citing a single unrefereed report of SPECT data as evidence (Jauss et al 1994). Finding no such data for patients with catatonia, and citing elevated plasma HVA which he believes reflects mesolimbic and mesocortical dopaminergic pathways, he urges us to speculate that the involved pathways in NMS and catatonia differ. He presents additional findings from his own experiments which he interprets as showing alterations in the supplementary motor area, the anterior cingulum, and the dorsolateral prefrontal cortex in patients with catatonia. While he may be correct, the data are surely insufficient to credit these suggestions as more than anticipatory hopes.

Our argument that NMS be viewed as a type of catatonia is based on clinical symptomatology, course, and the effects of treatments. The association is presented to encourage clinical trials with the treatments for catatonia in those patients with signs of NMS who fail to respond to removal of the offending agents and supportive measures alone. We seek to treat patients with NMS 'as if they had catatonia', in the belief and experience that such an attitude is clinically useful.

The unitary argument also encourages the search for a common pathophysiology. Observations that sedative drugs and ECT relieve both catatonia and NMS argue for a commonality in the central mechanisms of action between these treatments. Their antiepileptic activity and their influence on central gamma-aminobutyric acid come to mind.

Dr. Northoff's experiments are important additions to the ongoing discussion of motor syndromes in patients with mental disorders. A further exploration of these questions in a German symposium adds new thoughts and in one essay, an author again argues for the similarities between NMS and catatonia (Wähner 1995).

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Monoamine Oxidase, Tobacco Smoking, and Psychiatric Disorders

To the Editor:

Berlin and colleagues (1995) have made an important contribution to knowledge by showing that tobacco smokers have about 24% lower monoamine oxidase (MAO)-A and about 53% lower MAO-B activity than nonsmokers. Their study further extends animal (Boulton et al 1988; Essman 1977; Yu and Boulton 1987) and human (Oreland et al 1981; Norman et al 1982, 1987) studies of MAO inhibition by tobacco smoke. Very recently, Fowler et al (1996) found that brain MAO-B is about 40% decreased in tobacco smokers compared to nonsmokers when deuterium substituted [^{11}C]L-deprenyl is used as a positron emission tomography (PET) ligand. The sum total of all of these reports is relevant to a number of psychiatric disorders in addition to those mentioned by Berlin et al. The platelet MAO-B story in schizophrenic patients is an especially valuable lesson to all involved in biological psychiatry. I recently had a literature search run on the databases from 1966 to 1995 from the National Library of Medicine and the National Cancer Institute on the combination of the terms monoamine oxidase (MAO) and schizophrenia. A total of 165 literature references were identified. The literature is replete with contradictions. A meta-analysis by Marcolin and Davis (1992) indicates that when schizophrenic patients were given a neuroleptic their platelet MAO activity was lower than mentally normal control subjects. Platelet MAO activity in most drug-free schizophrenic studies was similar to controls. Only a minority of studies found that platelets from drug-free schizophrenic patients had decreased MAO levels. Our own research (Domino and Khanna 1976) was one of the first to indicate that "drug-free" male schizophrenics had reduced platelet MAO activity and a prolonged whole blood