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Periodic catatonia: a schizophrenic subtype with major gene effect and anticipation

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Abstract In a family study involving 139 probands with DSM-III-R catatonic schizophrenia and 543 first-degree relatives, we investigated age-specific morbidity risk according to Leonhard's clinical distinction between systematic and periodic catatonia. This dichotomy is based on different types of symptomatology, course, and outcome. In systematic catatonia the age-corrected morbidity risk was 4.6%. In periodic catatonia, however, there was an age-corrected morbidity risk with homogenous psychoses of 26.9%, and more parents than siblings were affected. This points strongly to a major gene effect in periodic catatonia. Furthermore, a pairwise comparison of patients and their parents revealed patterns of anticipation, i.e., the probands' age at the onset of disease was significantly earlier than that of their parents ($P < 0.001$). Similarly, anticipation was apparent in pedigrees with three successive generations affected. This inheritance pattern with homogenous psychoses and anticipation indicates that genes with trinucleotid repeat expansion or other repetitive elements affecting gene expression may be involved in the etiology of periodic catatonia. Thus, periodic catatonia as a specific clinical subtype of schizophrenia is a promising candidate for molecular genetic evaluation.

Key words Schizophrenia · Periodic catatonia · Inheritance · Anticipation · Leonhard classification

Introduction

Anticipation refers to the unusual pattern of genetic disorders whose age of onset is progressively earlier in successive generations. This phenomenon, however, tended to be discounted as a biased assessment (Harper et al. 1992). Recently, the discovery of a new form of human mutation provided a specific biological explanation for several inherited diseases with anticipation. In Huntington's disease, myotonic dystrophy, fragile X-syndrome, spinocerebellar ataxia (SCA 1), and dentatorubral-pallidoluysian atrophy (DRPLA) unstable expansions of trinucleotide repeats were identified in coding/noncoding regions of distinct genes. Repeat length and instability were directly associated with earlier age of onset in successive generations (Ross et al. 1993).

Besides the current psychiatric classification systems (in DSM-III-R), Leonhard (1979) classified schizophrenia between systematic and unsystematic forms based on different types of symptomatology, longterm course, and outcome. This highly operationalized classification system is of outstanding validity and reliability (Astrup 1979; Lindvall et al. 1986; Trostorff and Leonhard 1990; Franzek and Beckmann 1992; Warkentin et al. 1992; Ungvari 1993). Periodic catatonia is one clinical subtype of unsystematic schizophrenia. Its course is typically bipolar in both hyperkinetic as well as akinetic states. Characteristically, symptoms of one pole are mingled with those of the other. The distortion of psychomotor activity leads to grimaces, parakinetic movements, stereotypes, impulsive actions with aggressiveness, and negativistic behavior. This polymorphous catatonic symptomatology is manifest in remittent course. After one or more attacks residual states develop with increasing poverty of movements, blunted affect, and lack of motivation. In contrast, systematic catatonias usually begin insidiously and run a chronic, progressive course without remissions. The irreversible, treatment-resistant residual states of systematic catatonias are clinically well-defined and can be reliably distinguished from periodic catatonia (Franzek and Beckmann 1992). Leonhard reported that the heredity pattern of systematic catatonia is significantly different from that of periodic catatonia. For systematic catatonia he found a positive family history with regard to schizophrenia in 3–4% of patients, whereas approximately 20% with periodic catatonia had a familial loading with homogenous psychoses.

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As one part of an extensive family study on systematic and periodic catatonia, we investigated familial aggregation of psychoses among all first-degree relatives for both diseases. We explored the occurrence of anticipation in periodic catatonia and discussed the results with regard to the recent findings on trinucleotid repeat expansions affecting gene expression.

Subjects and methods

Recruitment of patients and diagnostic assessment

Probands were drawn from all consecutively admitted inpatients and from outpatient care at the Department of Psychiatry Wuerzburg University and from wards with chronically ill patients at the Lohr/Main State Hospital. Patients were recruited from April 1991 to October 1992. As a first step, one of us (G.S.) screened the hospital records of 749 patients as to whether they had displayed catatonic symptoms cross-sectionally and/or in the long term. A total of 183 patients exhibited catatonic features at least once during their illness. These patients were personally examined by two experienced psychiatrists (E.F. and H.B.) independently working and diagnosed along the lines of Leonhard's nosology. The case notes that were at their disposal did not contain any information about familial affliction. In a subsample of 32 patients both investigators had a coefficient of agreement of 0.93 (Cohen's Kappa) within Leonhard classification. This corresponds to the high interrater reliability of a previous study (Franzek and Beckmann 1992). Of the 183 patients, 44 did not fulfill diagnostic criteria of either systematic or periodic catatonia. Thus, the final diagnostic group consisted of 139 probands. All of them met the diagnostic criteria of schizophrenia of the catatonic type according to DSM-III-R. There were 83 patients (42 males and 41 females) with periodic catatonia and 56 patients (42 males and 14 females) with systematic catatonia. In periodic catatonia the mean age at the time of assessment was 46.5 years (SD ± 16.8 years). The mean duration of the disease was 22.7 years (SD ± 15.0 years). The mean age at first hospitalization was 24.8 years (SD ± 9.6 years). Men were insignificantly younger up on their initial hospitalization (23.2 years; SD ± 8.0 years) than women (26.5 years; SD ± 10.8 years).

In 56 patients with systematic catatonia the mean age at the time of study was 40.7 years (SD ± 14.1 years). The mean duration of the disease was 21.0 years (SD ± 13.7 years), and the mean age up on initial hospitalization was 20.8 years (SD ± 7.0 years) with no difference in age up on initial hospitalization between women (20.7 years; SD ± 7.8 years) and men (20.8 years; SD ± 6.9 years).

This study was approved by the appropriate ethics committee and was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

Evaluation of morbidity risk in first-degree relatives and anticipation

In order to get reliable data concerning morbidity risk, age at first hospitalization, and familial psychopathology, we only allocated relatives with documented psychiatric hospitalization to the group of affected family members. Hospital records were available for all these relatives. Extensive pedigree data were conducted on each patient's family. In order to exclude multiple ascertainment, consecutively admitted members of a proband's family were not considered as probands. The multiinformant family psychiatry history was not applied in this report (Weissmann et al. 1986).

Definition of the age of onset in mental illnesses is a matter of debate (DeLisi 1992). Because of the fact that all hospital records could be traced, we decided to use age up on initial hospitalization to define age of onset. This is a rather conservative approach defining the age of onset. However, periodic catatonia usually begins with acute and severe hyperkinetic or akinetic attacks that nearly always lead to hospitalization (Astrup 1979; Franzek and Beckmann 1992). Therefore, in most cases of periodic catatonia the time of first hospitalization coincides with the time of the onset of disease. Systematic catatonia, however, begins insidiously in most cases. Therefore, age of onset of the systematic catatonic probands may be lower than estimated with this method.

In order to analyze anticipation (progressively earlier age of onset in successive generations), we included only probands with definite unilineal parental transmission. Patients whose parents were both affected were excluded. The appearance of anticipation in these patients might be the result of an additive effect of disease genes from both parental lines.

Statistical methods

A difficult statistical problem in family studies is the fact that relatives do not constitute strictly independent data points. This has remained unresolved in recent family studies on schizophrenia (Kendler et al. 1993; Maier et al. 1993). In this report we also decided to consider the generations as one group of relatives for each schizophrenic subgroup. The life-table analysis was used to examine age-specific morbidity risk (Kaplan-Meier estimates). The difference in life-table curves was determined by the log-rank χ^2 statistic with 1 *df*. Pairwise intergenerational differences (age at first hospitalization among parents and probands) were compared using nonparametric Wilcoxon matched-pairs statistics and Spearman rank correlation.

Results

Life-table analysis of morbidity risk in first-degree relatives

Figure 1 shows that the age-specific morbidity risk for schizophrenia was substantially greater for first-degree relatives of patients with periodic catatonia than for patients with systematic catatonia. Probands with systematic catatonia had 220 first-degree relatives (parents and siblings). Four of 109 parents and 3 of 111 siblings were afflicted. The age-corrected morbidity risk for relatives of systematic catatonic patients was at a level of 4.6%. Probands with periodic catatonia had 323 first-degree rel-

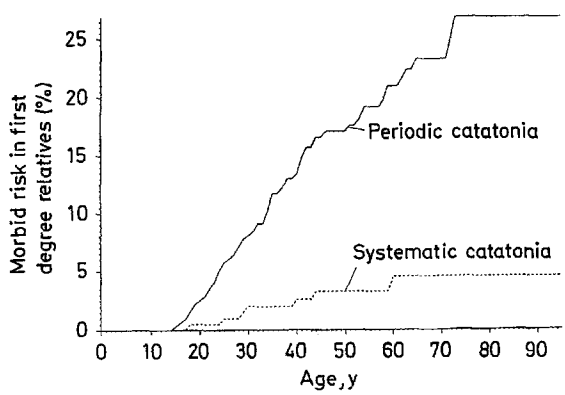

Fig. 1 Morbidity risk in systematic catatonia and periodic catatonia. Systematic catatonia revealed no evidence of increased familial aggregation in schizophrenia in 220 first-degree relatives. The age-corrected morbidity risk was 4.6%. In contrast, periodic catatonia followed a pattern of dominant inheritance. The age-specific morbidity risk among 323 first-degree relatives was 26.9%, and there were more affected parents than siblings. The morbidity risk in the two schizophrenic subgroups was different at a level of $P<0.0001$ (life-table analysis)

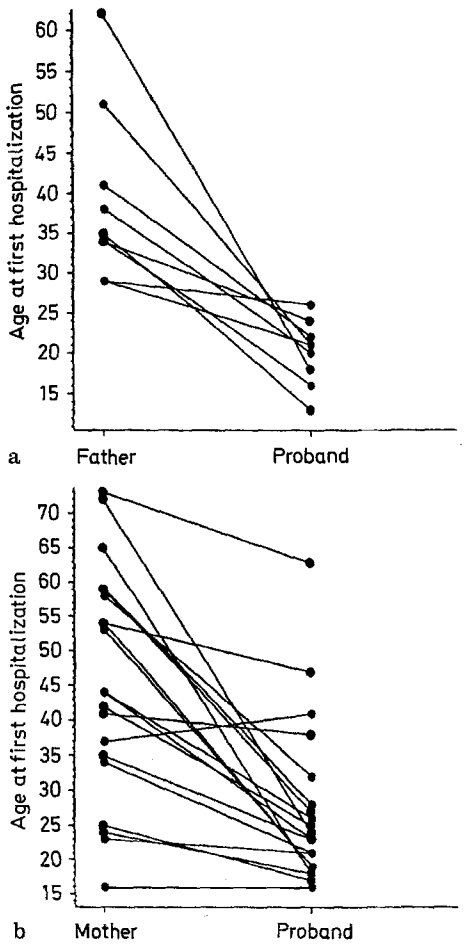

Fig. 2 a, b Unilineal paternal transmission. **a** (n = 9): Probands had a significantly earlier age of onset with a mean age of 20.1 years (SD ± 4.0 years) compared with their fathers with a mean age of 39.2 years (SD ± 10.9 years; $P < 0.01$). **b** (n = 20): Probands had a significantly earlier age of onset with a mean age of 27.3 years (SD ± 11.9 years) compared with their mothers with a mean age of 45.6 years (SD ± 16.5 years; $P < 0.001$)

atives. Of them 63 received treatment in a psychiatric hospital. Case notes from 4 of the 63 relatives revealed no definite schizophrenic symptomatology. This resulted in 59 of 323 relatives with a definite diagnosis of schizophrenia. The age-corrected morbidity risk for first-degree relatives was 26.9%. The difference in the morbidity risk between systematic and periodic catatonia was statistically highly significant ($P < 0.0001$).

In contrast to systematic catatonia, periodic catatonia revealed pronounced vertical transmission. Of 161 parents 33 (20.5%), and 26 of 162 siblings (16.0%), were afflicted (n.s.). This vertical transmission with more afflicted parents than siblings points to a major gene effect (Vogel and Motulsky 1986; Propping 1989).

Anticipation in periodic catatonia

Thirty-one probands had a total of 33 affected parents. In 2 patients both parents were affected. Thus, the measure

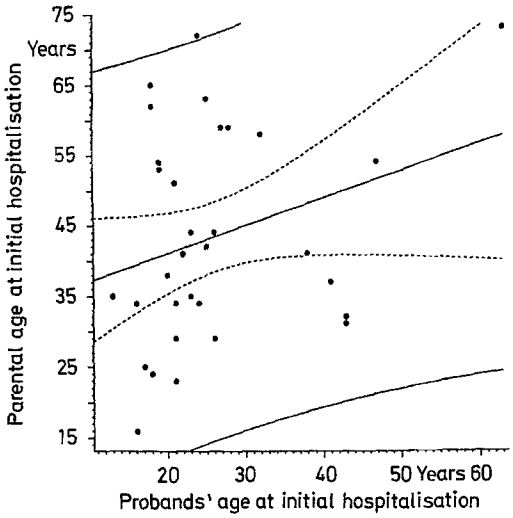

Fig. 3 Correlation of probands' age of onset and parental age of onset in periodic catatonia (n = 33): There was no linear relationship between age at initial hospitalization in probands and their parents (r = 0.2836; n.s.; Spearman rank correlation). Anticipation is clearly apparent in probands with early-onset parents (< 30 years) indicating that true anticipation occurred

of anticipation is based on 29 proband-parent pairs. In pairwise comparison patients showed a significantly earlier age of onset (mean age 25.1 years; SD ± 10.6 years) compared with their parents (mean age 43.6 years; SD ± 15.1 years; $P < 0.001$). In 9 cases the disease was unilineally paternally derived (Fig. 2a). The fathers had a mean age of onset of 39.2 years (SD ± 10.9 years), and the successive generation fell ill at a mean age of 20.1 years (SD ± 4.0 years). All probands exhibited an earlier onset than their fathers ($P < 0.01$). In 20 cases the disease was unilineally maternally derived (Fig. 2b). The mothers' mean age of onset was 45.6 years (SD ± 16.5 years), and their offspring fell ill at a mean age of 27.3 years (SD ± 11.9 years). In 18 of 20 mother-proband pairs earlier age of onset could be observed in the successive generation ($P <$ 0.001). In one pair both fell ill at the age 16 years, and in one pair the proband was older at the onset of disease (41 years) than his mother (37 years). In our sample 21% of the parents (6 of 29 cases) showed onset < 30 years. Progressive earlier onset in the offspring was evident in 5 of these early-onset parents. Anticipation varied from 2 to 8 years. In one pair both had the initial hospitalization at the age 16 years. Furthermore, episode frequency increased from 5.8 (SD ± 4.3 years) among probands compared with 3.5 (SD ± 3.7 years) among parents ($P < 0.05$). This indicates that genetic anticipation is present.

Figure 3 shows that there was no linear correlation between age of onset in probands and their parents (r = 0.2836, n.s.; Spearman rank correlation). Furthermore, age of onset was not normally distributed around the mean.

In systematic catatonia the 4 affected parents exhibited a later mean age of onset of 41.5 years (SD ± 13.3 years) compared with 22.3 years (SD ± 10.1 years) in the probands, but 1 parent (25%) definitely had an earlier onset than the offspring. It was only logical that in system-

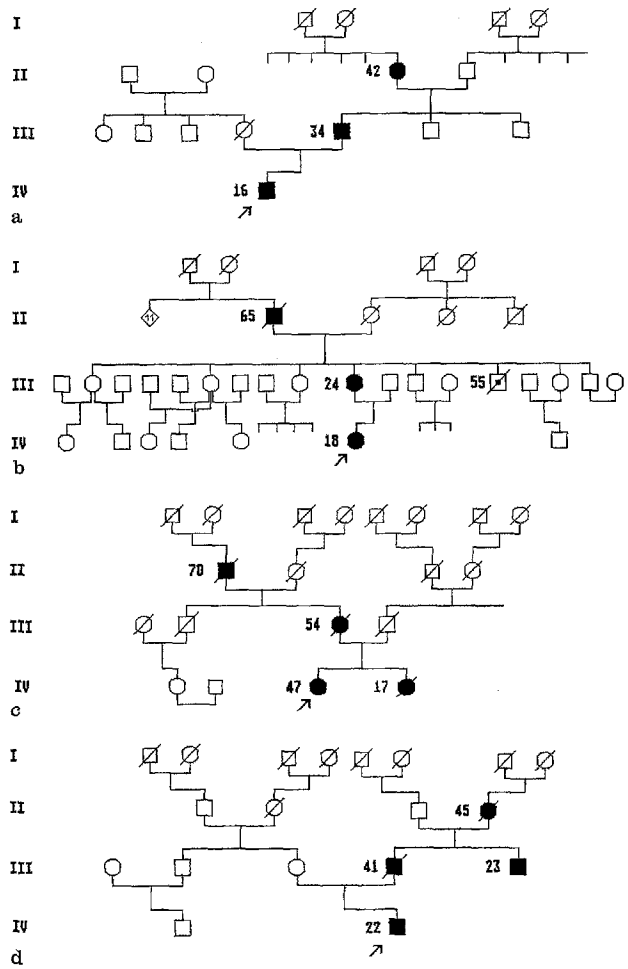

Fig. 4a–d Periodic catatonia and anticipation: Family pedigrees from probands with periodic catatonia extending over three successive generations with a progressively earlier age of onset in each generation. *Circles* represent female patients, *squares* male patients, *slashed symbol* a deceased individual, *target symbol* suicides, *solid symbols* patients who received hospital treatment for periodic catatonia, and *arrows* the probands. The ages shown are the ages up on initial hospitalization

atic catatonia with early onset and chronic progressive course parents exhibit a later onset than their offspring.

Anticipation in extended pedigrees of periodic catatonia

Figure 4 depicts the appearance of anticipation in four representative extended pedigrees. Periodic catatonia occurs in three successive generations. In family A the age of onset decreased from 41 years (II) to 34 years (III) to 16 years (IV). Family B exhibits anticipation with the onset at 65 years (II), 24 years (III), and 18 years in the proband (IV). In family C the age of onset decreased progressively from 70 years (II) to 54 years (III) to 47 and 17 years in IV. Family D shows anticipation with the age of onset at 45 years in II, 41 years in III, and 22 years in IV. Brief case notes in the *Appendix* illustrate the homogeneity of symptomatology, course of the diseases, and progressively serious disease development in successive generations.

Discussion

Morbidity risk for first-degree relatives in systematic catatonia, periodic catatonia, and familial psychopathology

The familial aggregation of schizophrenia was statistically significantly different in specific subgroups of 139 patients with chronic schizophrenia, catatonic type, according to DSM-III-R. Applying Leonhard's classification (Leonhard 1979), 83 patients (59.7%) suffered from periodic catatonia with acute hyperkinetic or akinetic shifts, parakinetic distortion of movements resulting in residuals with poverty of movements, apathetic affect, and a decline in drive and motivation. A total of 56 patients (40.3%) were diagnosed as systematic catatonics with chronic nonremitting course and clinically well-defined residual states that were irreversible, unchangeable, and completely resistant to neuroleptic treatment (Beckmann et al. 1992).

There was a low morbidity risk (4.6%) among first-degree relatives of patients with systematic catatonia. Only 7 of 220 relatives were affected with a definitive schizophrenic disorder (Fig. 1). This corroborates the hypothesis that systematic catatonias are sporadic forms of schizophrenic psychoses (Leonhard 1979). In a previous study systematic schizophrenia was shown to coincide with an excess in maternal infectious diseases during midgestation (Stöber et al. 1992, 1994). There may be a link between exogenously induced disturbances of prenatal brain maturation and the development of schizophrenia in adulthood (Jakob and Beckmann 1986; Beckmann and Franzek 1992).

Some earlier studies (Slater and Cowie 1971; Scharfetter and Nuesperli 1980; Propping 1989) reported on increased familial occurrence of catatonic psychoses compared with paranoid or hebephrenic schizophrenia. The results of the present study suggest that this is confined to the clinical subtype of periodic catatonia according to Leonhard's classification. In agreement with Leonhard's findings (Leonhard 1979) we found high familial aggregation in periodic catatonia. The age-corrected morbidity risk in first-degree relatives was 26.9%. Recent family studies on schizophrenia (Maier et al. 1993; Kendler et al. 1993) registered only a small quota of parents affected (1.1 and 1.3%, respectively). In contrast, periodic catatonia shows an unequivocal familial aggregation of affected parents. No less than 33 parents of 83 periodic catatonic patients were hospitalized for definitive schizophrenic psychosis.

Kendler et al. (1994) argued that it is unlikely to find relationships between psychopathological patterns in probands and their relatives in schizophrenia. However, there was strong homogeneity in the symptoms and course of disease in periodic catatonia among first – and second-degree relatives. The characteristic syndrome of the disease was unequivocally present in schizophrenic pedigree members of three succeeding generations *(see Appendix)*. Thus,

periodic catatonia seems to be a well-defined clinical entity with a homogenous psychopathological picture in familial transmission. A high morbidity risk of 26.9% in first-degree relatives and pronounced vertical transmission (more parents than siblings are affected) point to a major gene effect (Vogel and Motulsky 1986; Propping 1989).

Anticipation in periodic catatonia

Anticipation refers to the earlier age of onset of inherited disorders in successive generations, i.e., Huntington's disease, myotonic dystrophy, fragile X-syndrome, and spinocerebellar ataxia. The molecular basis of anticipation is brought about by unstable expansions of trinucleotide repeats in distinct genes (Mandel 1993). McInnis et al. (1993) noted that anticipation occurs in the bipolar affective disorder. Asherson et al. (1994) rejected that true anticipation occurs in schizophrenia as one disease entity. One major bias that may have affected their results is that the pedigrees were identified for linkage analysis and consisted of multiply affected families with different diagnoses. Furthermore, they used data points more than once considering proband – parent as well as affected sibling – parent pairs, and calculated their data under the assumption that the age of onset shows normal distribution.

In our family study anticipation appeared in 27 of 29 (93%) periodic catatonic families with homogenous psychoses and unilineal transmission. Anticipation was present regardless of whether the disorder's derivation was maternal or paternal (Fig. 2). It is noteworthy that in unilineal transmission only one proband had a later age of onset than the parent (37 years compared with 41 years). Anticipation was clearly evident in the group of parents with early onset. Probands with early-onset parents (n = 6) showed further decline of age of onset compared with their parents. This provides evidence that genetic anticipation occurred. Contrary to Asherson et al. (1994), we were unable to find a simple linear relationship between age of onset in probands and parents (Fig. 3). Furthermore, data from extended family pedigrees substantiate the fact that anticipation occurs not only in two generations; but also in three successive generations (Fig. 4). The age of onset decreased from generation to generation, with the severity of the disease increasing progressively.

The appearance of anticipation may be the result of several different observational biases. The set up of the study included systematic recruitment of probands with catatonic schizophrenia. Thus, evaluation was not influenced by assessment biases for genetic linkage studies (multiplex-affected families). Multiple ascertainment of families was avoided. Only relatives who had received treatment at a psychiatric hospital for schizophrenic psychoses were classified as being affected. All records were available. In order to minimize the possible effect of disease genes from both parental lines, two bilineal families were dropped from the analysis of anticipation. Among families with unequivocal unilineal transmission no secondary cases of endogenous psychoses could be traced along the lines of nonaffected parents. We only considered proband-parent pairs. Affected sibling-parent constellations were disregarded, so as not to use data points more than once. The age of onset was taken as the age up on initial hospitalization. We chose this conservative approach to define the age of onset, because periodic catatonia usually leads to (emergency) hospitalization, due to severe and acute psychomotor disturbances. In 6 of 29 families (21%) the probands fell ill prior to their parent. At the time of admission their parents were described as being mentally healthy. One main bias is the preferential ascertainment of parents of late age of onset, because earlier age of onset might have caused diminished fertility. Our study included a sufficient number of early-onset parents. The offspring of parents with early-onset (< 30 years) unequivocally showed further decrease in the age at initial hospitalization just as those with late-onset parents (> 30 years). Thus, anticipation was not accounted for by the effect of advanced parental age of onset. Furthermore, anticipation of periodic catatonia in three consecutive affected generations provided evidence that the earlier age of onset in successive generations is not simply a phenomenon arising from reduced fertility of early-onset schizophrenics.

In conclusion, a dominant inheritance pattern in homogenous psychoses and anticipation may implicate genes with trinucleotid repeat expansion or other repetitive elements affecting gene expression (Li et al. 1993; Baron et al. 1994; Stöber et al. 1994; Lesch et al. 1994). Thus, periodic catatonia is a promising candidate to screen for abnormalities in genes with tri- and oligonucleotide repeats.

Appendix

Family A

Proband, born in 1961. Admitted acutely psychotic at the age of 16 years with stiff psychomotility and incomprehensible, distorted gestures. Speaks in a monotone and agrammatically; stereotype answers. Talks of delusions of persecution and in phonemes. Twelve catatonic attacks with severe psychomotor agitation, grimacing, nonharmonious, spiralling movements, bizarre finger motions, resistance, cenesthesic hallucinations, abstruse ideas and fantasies of self-grandeur, which invariably subside rapidly. Never gainfully employed. Accommodated in a sheltered home for 14 years. Periodic catatonia with severe lasting effects.

The father, born in 1938, a merchant. Suddenly becomes depressive at age 34 years. Negativistic/catatonic when admitted. Decline in moroseness and more approachable after 10 weeks. Remains chronically ill, complaining in a monotone of vitality deficiency, lack of drive, physical weakness; occasional psychomotor excitation; socially reserved. Twenty-two years after the commencement of the illness, there is slight/medium-grade residual effects of periodic catatonia.

The grandmother, born in 1915. After giving birth, the 41-year-old, who to date has been healthy, experiences anxiety conditions. Admitted as an inpatient she weeps without being depressive; monotonous, hypochondriacal complaints. Poverty of movement with parakinetic bodily twitching. Occasionally catatonic/stuporous. Stereotype wailing, grimacing. Released after 6 months with the diagnosis of residual schizophrenia. After 37 years of illness, the September 1993 examination revealed moderate residual periodic catatonia with parakinetic facial movements, nonharmonious, jerky gait, and speech in a monotone, apathetic affect.

Family B

Proband, born in 1967. Acute commencement of illness at age 18 years: runs around aimlessly, twitches all over her body, laughs for no reason. Later lies in bed akinetically, staring blankly; then again excited, pushing; ideas of reference. One year later again excited; lively, nonharmonious movements. Verbigeration, brief paranoid-hallucinatory symptoms. Third time of admission: abrupt, jerky movements, remaining in uncomfortable positions; suddenly becomes extremely excited for no reason. Remission of acute symptomatology; typical residual effects of periodic catatonia with adynamia, poverty of movement, and nonharmonious psychomotility.

The mother, born in 1935, a worker. Admitted at 24 years after attempting suicide: substuporous/negativistic, delusions of persecution; then excited, distorted facial expressions, and groundless giggling to herself. Ten catatonic attacks with stupor and excitation: stands crookedly and motionlessly with raised hands; grimaces; lies stiffly, flailing simultaneously with her legs. Verbigeration, forced laughter, and occasional phonemes. During examination November 1993; there is evident residual effects of periodic catatonia with jerky movements, parakinesis of the face, general reduction in drive, and affective apathy.

The grandfather, born in 1906, a farmer. Becomes acutely psychotic at the age of 65 years and is admitted in a state of catatonic agitation (jumps around the ward extremely excited and waving his arms, stereotype yells), ideas of reference. Two subsequent admissions: once in an akinetic/substuporous state; the second time excited and hallucinating. Rapid remissions each time, no evident residual effects. Dies in 1977 as a result of a cerebral fit.

Family C

Proband, born in 1926. Gainfully employed until a few months before admission; acutely anxious/depressive; continual inpatient since February 1973; rigid catatonic posture on admission, mutism, ambitendency; July 1982, catatonic/stuporous for weeks, negativistic, must be fed; in 1983 sits mutely, rejective; in 1989 excited, morose; then negativistic/stuporous. Examinations between 1990 and 1993 led to the same findings: lifeless facial expression, nonmodulated, jerky movements, apathetic affect, marked lack of drive: severe residual condition in periodic catatonia.

The sister, born in 1939. Acute commencement March 1956 (17 years old): stands around stiffly with stereotypical movements of the arms; turns away when spoken to. May 1956; extremely excited for weeks: shivers, fidgets with clumsy, distorted dancing motions, grimaces, sniffs, blows, opens her mouth wide, and rips clothing. Long-lasting hyperkinetic states during four further times of inpatient treatment, later increased akinetic/stuporous attacks. In examinations in 1990 the patient lies stiffly in bed with parakinetic agitation of the extremities and face; short, agrammatical answers. Very severe final condition of periodic catatonia. Dies in 1991 from mesenteric vein thrombosis.

The mother, born in 1902. Falls ill in 1956 at age 54 years, at the same time as the daughter. Up admission in a state of catatonic excitation with distorted movements, alternately praying, singing, and yelling. Then akinesis with blank facial expression, staccato speech. After a short period of improvement again excited, stereotypical yells, rolls around with jerky movements in bed. After release apathetic and low in drive. Severe attack of periodic catatonia; mild subsequent residual effects. Dies in 1970.

The grandfather, born in 1867, a farmer. At the age of 70 years, suddenly occurring psychomotor excitation lasting for weeks, aimless wandering, delusions of persecution, and phonemes. Subsequently, lack of drive lasting for months. No indication of organic causes. Thereafter psychologically healthy; dies at age 86 years. A mild attack of catatonia without evident residual effects.

Family D

Proband, born in 1967. After the father's death, acute anxious condition and ideas of reference at the age of 22 years. On admission akinesis with distorted facial movements, ambitendency, and monosyllabic replies. Subsequently, extreme excitation with jerky, hurried running around; rolls around in bed with distorted movements, ripping clothing. Since then, several mild catatonic attacks, short-term ideas of reference. January 1994, morose mood during renewed further examination. Stiff, jerky movements; rigid facial expression, nonmodulated. Little social contact; works hourly under supervision. Moderate residual effects of periodic catatonia.

The father, born in 1939, an academic. In 1975 anxious/depressive, alcohol abuse. At the age of 41 years, he became acutely ill, running around hastily and jerkily, flight of ideas, hears voices from the cosmos. Then irritated, reluctant. On subsequent admissions hyperkinetic pole of periodic catatonia (excited, pummelling the walls with his fists, ripping the clothes from his body, excessive facial expression and gestures) in addition to the inhibited pole with parakinetic intermixtures (lies mutely in a rigid posture, flapping his arms). Anxious ideas of reference. Increasing adynamic residual effects. Dies of myocardial infarction in 1989.

The father's brother, born in 1948. Apprenticeship completed. He is 19 years of age up on admission: excited/rejective; ambitendency, paralogia, and lively grimacing. Later endlessly disinhibited, aggressive, delusions of grandeur, clumsy, and mannered psychomotility. Within a few years severe adynamic residual symptoms with impulsive excitation. Long-term hospitalization. Sixteen catatonic attacks: sits for days swaying his torso back and forth, mute; then dysphoric/excited, psychomotor agitations, phonemes, ideas of reference. February 1994, very lethargic according to the doctors treating him, friendly/apathetic affect: severe residual effects of periodic catatonia.

The grandmother, born in 1912. Suddenly anxious at age 45 years, feeling persecuted. Up on admission extremely excited, rejective; then staring mutely, stereotypical swaying of her head. Euphorically excited at age 47 years, distorted, nonharmonious movements, phonemes with religious content, perseverations; then rejective/stuporous, stiff psychomotility. Released 8 months later: drive paralyzed, apathetic affect. One year later catatonically excited, grimacing, pulling her hair, with extremely distorted grimacing, vocally excited, uttering stereotypical sentences. Dies at age 51 years from a pulmonary embolis during a relapse of the illness.

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