

Periodic Motor Impairments in a Case of 48-Hour Bipolar Ultrarapid Cycling before and under Treatment with Valproate

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Key Words

Ultrarapid cycling · Handwriting · Digitizing tablet ·
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Abstract

Motor impairments of psychiatric patients can be assessed with digital recordings of handwriting tasks. The investigation of patients with bipolar affective disorders differentiates intraindividual changes related to the patient's fluctuating affective states. An unmedicated 67-year-old male with 48-hour bipolar ultrarapid cycling was investigated during 8 consecutive days of ultrarapid cycling and 4 weeks later, after remission under treatment with valproate. The handwriting skills of the patient followed the same rhythmic changes of the psychopathology in the first part of the study and a steady pattern in the second phase, after remission. Therefore, it can be assumed that the handwriting skills reflect a state marker of the disease. Poorer handwriting skills on the manic days, as compared to the depressive ones, support the hypothesis of a low arousal in manic patients.

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Introduction

Many groups of psychiatric patients show motor impairments which might reflect 'trait' markers or 'state' markers of the disease [1–3]. Acute depressive patients have shown fine motor retardations and impairments performing drawing and handwriting tasks, as compared to matched healthy controls. The patients were not only slower when writing sentences, letter sequences, their personal signature or drawing fast concentric circles, but also showed poorer skills with respect to the smoothness, or the degree of automatization, of their movements [4–6].

Through the investigation of diseases with rapid changing or cycling syndromes like bipolar affective disorders, an approach to the differentiation between traits and states is possible. The investigation of the same patients in depressive and manic states presents a unique natural experiment for the differentiation of intrapersonal differences, so-called states. The investigation of a patient with 48-hour bipolar ultrarapid cycling affective disorder [7] expedites this process even further.

Rapid cycling is defined in DSM-IV as at least 4 depressive and/or manic episodes, or 2 complete cycles, per year; ultrarapid cycling requires unipolar or bipolar cycles lasting for 48 h, i.e. 24 h of depressed state are followed by 24 h of an euthymic or manic state, and vice versa. The number of reported cases of ultrarapid cycling are very low (12 cases counted from 1808 until 1974 [8]; 8

additional cases until today). Nevertheless, the exact clock-like, periodic changes of the affective state provide good conditions for an investigation of the state markers of bipolar affective disorders.

Methods

A 67-year-old male was assessed during a period of 8 consecutive days without the influence of any medication and then 4 weeks later, under treatment with valproate. The patient was suffering from 48-hour bipolar ultrarapid cycling (DSM-IV 296.80), where 24 h of a depressed state were followed by 24 h of a manic state and vice versa. The onset of the disease was at least 5 years ago. Based on the doubtless clinical impression, the first diagnosis of an outpatient clinic was confirmed in the psychiatric hospital of the University of Munich. The patient has been treated with various psychopharmaca without any success, including lithium in clinically relevant doses over a long period of time.

Up until the first 8 days of the investigation, the patient was free of psychotropic or other medication for at least half a year. After the first phase of the investigation, the patient was treated with valproate at increasing doses. The dose of 1,800 mg/day during the second phase of the investigation led to a plasma level of 85.7 µg/ml (therapeutic range: 50–120 µg/ml).

In addition to clinical and self-ratings for the psychopathological states, the handwriting skills of the patient were also examined. The psychopathological states were assessed by adding the score of all items of the Bech-Rafaelsen-Melancholia Scale and the Bech-Rafaelsen-Mania Scale [9], respectively. For self-ratings, the patient was asked to fill out the visual analog scale [10].

The handwriting was recorded via a digitizing graphic tablet and in addition to various writing and drawing tasks, the patient had to write samples of the letters 'aaa' in 4 given sizes (6, 12, 18 and 24 mm). The required size was indicated by 2 horizontal lines. The daily investigation time was 11.00 a.m. during the first and the second phase of the investigation.

The digitizing graphic tablet worked with a special signal-processing software using a sampling rate of 200 Hz and a spatial resolution of 0.05 mm. The pen felt like and was used as a regular ballpoint pen to mark the trace on a regular sheet of paper which was lying on the digitizing graphic tablet. The pen transmitted electronic signals which were detected by the digitizing graphic tablet and forwarded to the computer. The trace of the tip of the pen on the paper and in the air up to a distance of 1 cm above the surface of the digitizing graphic tablet was recorded. Signal processing and the extraction of parameters for further investigation were done off-line. After the application of an algorithm for smoothing and noise reduction [11], the coherent pattern of letters or drawings was segmented into so-called 'strokes'. Each stroke represented a half cycle, with its borders defined by points of the graph where the vertical direction of the movement reversed; corresponding to infinitesimally short moments of zero vertical velocity. Various kinematic parameters, reflecting the dynamics (velocity, acceleration) and the smoothness and regularity of the movement were calculated for each stroke and subsequently averaged for statistical analysis [12].

Skilled handwriting is represented by highly automated movements. The degree of automatization was assessed by the number of inversions of the acceleration profile (NIA) for each stroke. Highly

automated movements show bell-shaped curves corresponding to monotonous acceleration before and monotonous deceleration after the velocity peak of every stroke within a continuous pattern [13]. In this ideal case, the acceleration profile shows one reversal, or change of direction, scored as NIA = 1.

Results

The handwriting skills of the patient showed pronounced periodic changes from day to day in the first phase of the investigation, when no medication was given. The systematic changes in the automatization of handwriting corresponded to the day-to-day fluctuation between the manic and depressed states (fig. 1a). The degree of automatization was indicated by the number of inversions or reversals of the acceleration profile.

On manic days, the automatization of the patient's handwriting was very poor, whereas the handwriting was smoother and more skilled on depressed days. These states are reflected by high numbers of inversions of the acceleration profile on the manic days (fig. 2) and fewer inversions or more bell-shaped curves on the depressed days (fig. 3). The segmentation of curves into strokes is indicated by vertical lines on the graphs of vertical position (fig. 2b, 3b), velocity (fig. 2c, 3c) and acceleration (fig. 2d, 3d) over time. In particular the graph of performance on a manic day (fig. 2d) shows a high number of inversions, i.e. number of local maxima and minima, between each pair of the dividing vertical lines. The high number of inversions reflects the poor automatization on that day, as compared to the fewer number of inversions between dividing lines on the depressed day (fig. 3d).

After 4 weeks treatment with valproate, the periodic change in the patterns of the automatization parameters of handwriting disappeared concurrently with the stabilization of clinical and self-ratings (fig. 1b). In this second phase of the investigation, the parameters stabilized in the same range observed on the depressed days before medication.

As in the case of the handwriting parameters, the psychopathology of the patient, as assessed by the Bech-Rafaelsen-Melancholia and Mania Scales, showed repetitive changes from day to day in the first phase of the investigation. The clinical ratings were in line with the self-ratings, on visual analog scales, both demonstrating regular shifts between manic and depressed days before medication. After 4 weeks of medication, the patient was nearly stabilized and remitted. In addition to subjective improvement reported by the patient, the rhythmic changes in clinical and self-ratings were no longer visible [7].

Fig. 1. NIA reflecting the degree of automatization of handwriting movements over days of observation. **a** Eight days with ultra-rapid cycling before medication, beginning of observation with a manic day. **b** Eight days after 4 weeks of valproate – No visible day-to-day fluctuation of the NIA parameter.

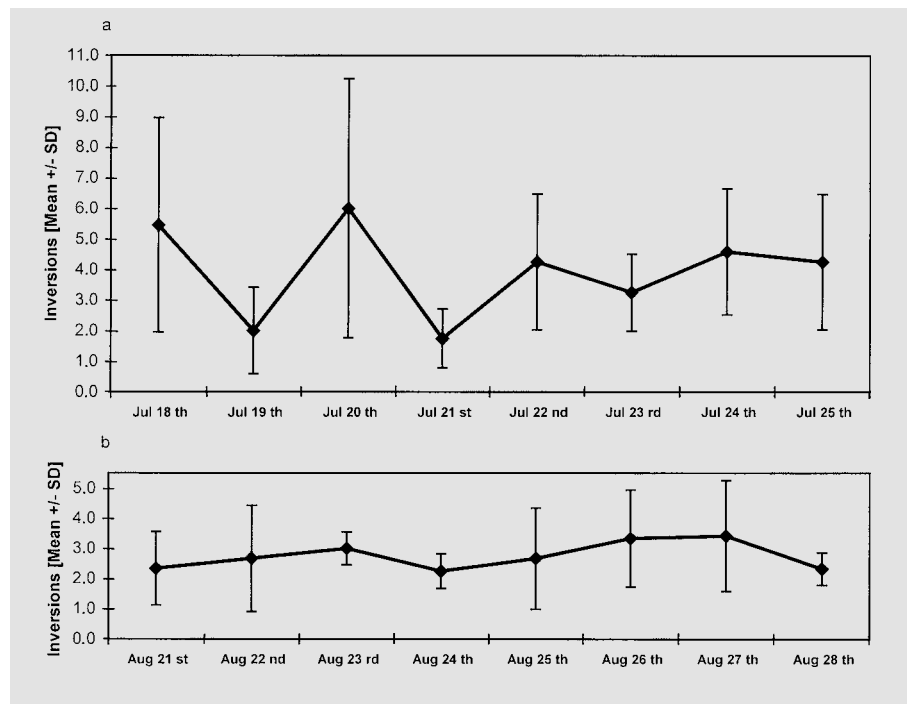


Fig. 2. Example of a letter sequence recorded on a manic day (day 3 of the first phase of the investigation). **a** X-Y position. **b** Vertical position (Y) over time (T). **c** Vertical velocity (VY) over time (T). **d** Vertical acceleration (AY) over time (T). Each segment (stroke) of the acceleration signal shows a high number of inversions (i.e. number of local maxima and minima).

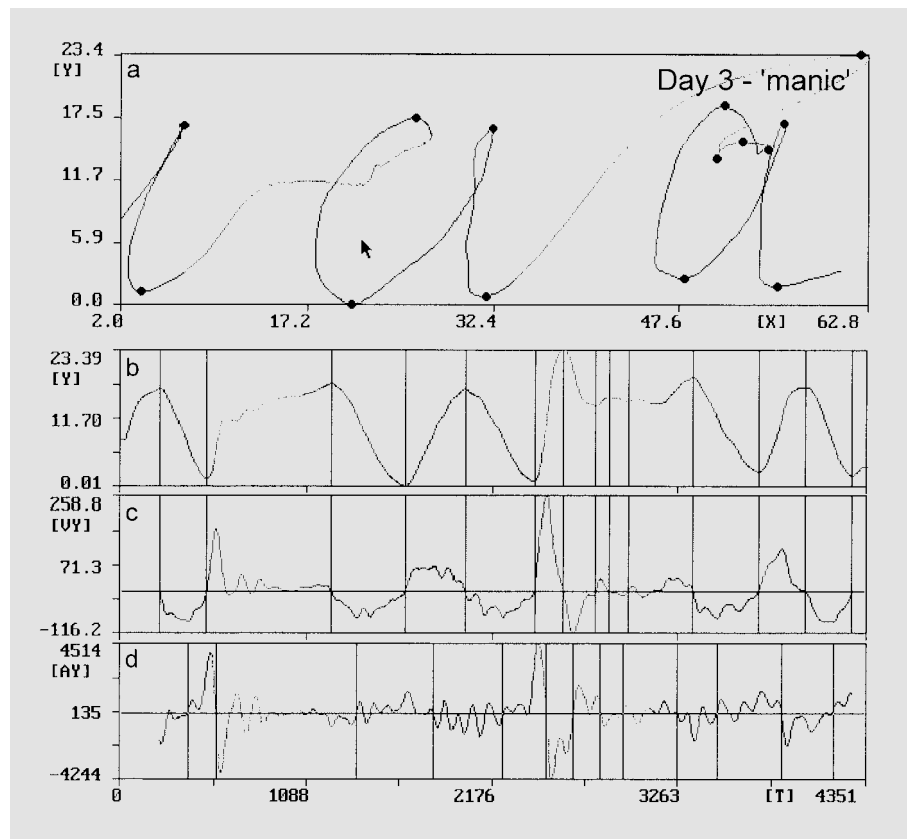


Fig. 3. Example of a letter sequence recorded on a depressed day (day 4 of the first phase of the investigation). **a** X-Y position. **b** Vertical position (Y) over time (T). **c** Vertical velocity (VY) over time (T). **d** Vertical acceleration (AY) over time (T). Each segment (stroke) of the acceleration signal shows fewer numbers of inversions (i.e. number of local maxima and minima) compared to the manic day.

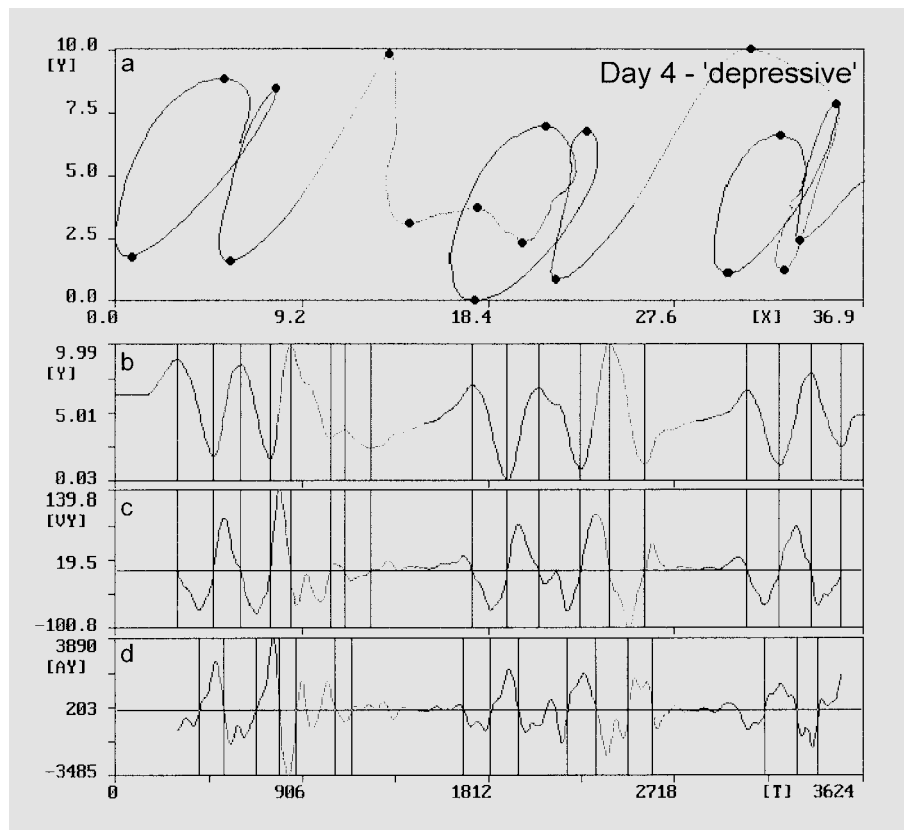
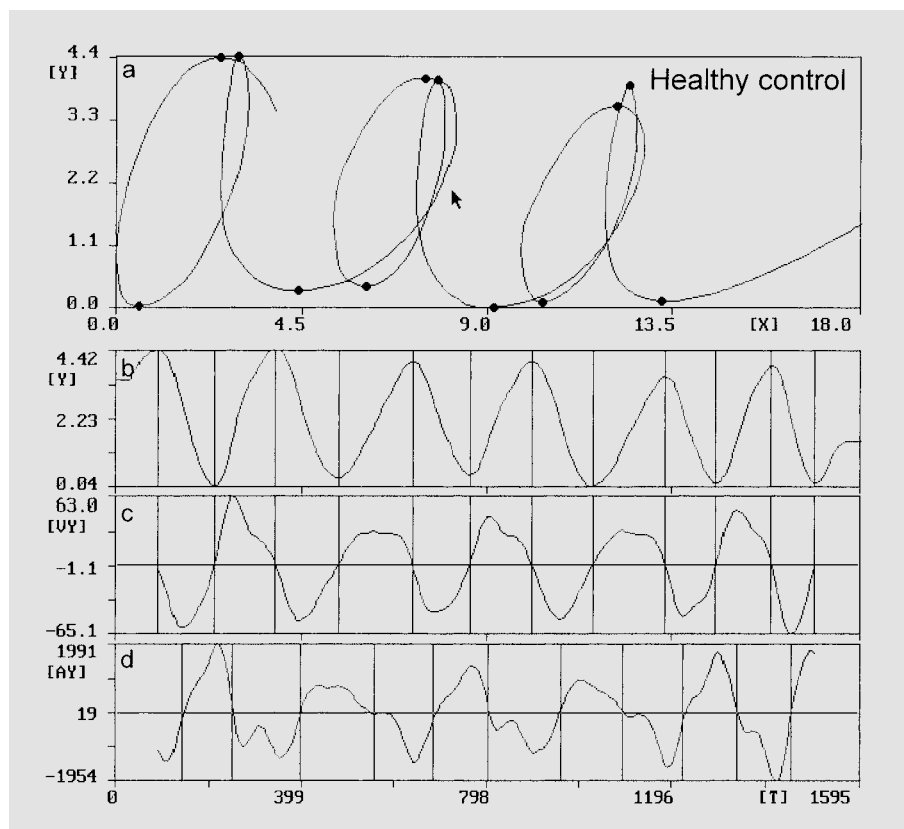


Fig. 4. Example of a letter sequence recorded from a healthy control. **a** X-Y position. **b** Vertical position (Y) over time (T). **c** Vertical velocity (VY) over time (T). **d** Vertical acceleration (AY) over time (T). Each segment (stroke) of the acceleration signal shows fewer numbers of inversions (i.e. number of local maxima and minima) compared to the recordings of the patient with 48-hour bipolar ultrarapid cycling.



Conclusion

Periodic changes in handwriting abilities, perhaps reflecting general motor impairments, paralleled the affective states of the patient. During the unmedicated phase of 48-hour bipolar ultrarapid cycling, handwriting parameters showed periodic changes from day to day. Handwriting skills were poor on manic days and were found to be better on depressed days, worsening again when mania returned.

The observed periodic pattern was assessed with an objective instrument during a phase of rapid periodic changes of affective states within the same patient. Therefore, the observed motor impairments obviously reflected a state marker of the disease and not a trait. In addition, parallel findings were made in biological and neurophysiological parameters, such as e.g. cortisol levels in blood or electroencephalographic activities [7].

The biological findings and especially the assessment of the handwriting abilities provide some implications for an understanding of the pathogenetic mechanisms generating affective disorders, since they trace the rhythmic changes of the psychopathological state in such patients.

The stabilization of the parameters for automatization under the treatment with valproate supports this view. Response to this treatment was accompanied by a stabilization of the parameters for automatization at the same level as observed on the depressed days before medication.

Interestingly, handwriting skills were less impaired on depressed days, as compared to during manic periods, even though, like skills of other depressed patients, they were worse than those of matched healthy controls (fig. 4). The worsening of automatization during mania may be related to a fast shifting of attention in manic patients, interrupting the concentration necessary for good performance on handwriting tasks. These findings support the hypothesis that manic patients are actually in a low state of internal arousal, and are able to maintain only low vigilance levels.

The parameters discriminated by the digitized assessment of handwriting abilities provide objective data for further investigation of psychiatric diseases, especially for the differentiation of mood-related states and the identification of trait markers of diseases such as bipolar affective disorders.

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