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Cycloid psychoses: Leonhard's descriptions revisited

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ABSTRACT – *Background and Objectives:* Cycloid psychoses are characterized by polymorphic symptomatology with intraphasic bipolarity, a remitting and recurrent course and favourable prognosis. Perris and Brockington (P&B) described the first set of operational criteria that were partly incorporated in ICD-10. The present study investigates psychopathological profiles according to the P&B criteria and the original descriptions by Leonhard, both against the background of the criteria from the prevailing international classification systems.

Methods: Eighty patients with psychotic disorders were recruited and assessed with various psychometric instruments at baseline and after six weeks of antipsychotic treatment in order to investigate the presence of cycloid psychoses according to Leonhard (LCP) and the effect of treatment with antipsychotics. The overlap between LCP and DSM-IV Brief Psychotic Disorder (BPD), ICD Acute Polymorphic Psychotic Disorder (APP) and P&B criteria was calculated.

Results: Using P&B criteria and a symptom checklist adapted from the original descriptions by Leonhard, 14 and 12 cases of cycloid psychosis were identified respectively reflecting a prevalence of 15-18%. Small though significant concordance rates were found between LCP and both DSM-BPD and ICD-APP. Concordance between LCP and P&B criteria was also significant, but modest.

Conclusions: This study demonstrates that LCP can be identified in a substantial number of patients with psychotic disorders. Cycloid psychoses are not adequately covered in current classification systems and criteria. Since they are demonstrated to have a specific psychopathological profile, relapsing course and favourable prognosis, it is advocated to include these psychoses in daily differential diagnostic procedures.

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Introduction

As an independent group, the term "cycloid psychoses" was first coined by Kleist in 1926[1]. Psychoses with atypical symptoms had been described from the turn of the nineteenth century and were termed e.g., "bouffées délirantes des dégenerées"[2], "Degenerationspsychose"[3], acute schizoaffective psychosis[4], "degeneratiepsychose"[5] and atypical psychosis[6]. About two decades ago, the psychopathological concepts about this type of psychoses were reviewed in detail by Tappe[7].

In general, cycloid psychoses present with a (sub)acute onset and a polymorphic and shifting symptomatology comprising symptoms from both the schizophrenic and affective spectrum. Depending on the subtype, most typical symptoms are rapid mood swings, severe anxiety and/or ecstasy, confusional states and psychomotor disturbances[8-11]. In the fifties, based on the detailed longitudinal analysis of symptom profiles, Leonhard delineated three subtypes: anxiety-happiness psychosis, confusion psychosis and motility psychosis[12]. Later, Pfuhlmann and coworkers found high inter-rater reliability (Cohen's kappa: 0.82-0.89) of Leonhard's classification system[13].

As to prognosis, cycloid psychoses show a remitting and recurrent course with a favourable outcome[14-16]. The only study on the pharmacological treatment of cycloid psychoses has demonstrated beneficial effects of lithium[17]. More recently, some evidence has been obtained that, in the acute phase, atypical antipsychotics may be useful[18].

Although in 1952 the first edition of the DSM comprised a psychotic disorder with atypical symptoms resembling some features of the cycloid psychosis (termed schizophrenic reaction, acute undifferentiated type), later versions did not cover this diagnostic category. In fact, Kraepelin's dichotomy increasingly dominated the categorical structure in the consecutive editions of the DSM so that in DSM-IV[19], only Brief Psychotic Disorder (BPD) and Schizophreniform Disorder with specifier "With Good Prognostic Features" partially cover the cycloid concept. This development and the increase of the clinical diagnosis of schizoaffective disorders resulted in a gradual loss of scientific and clinical interest for the cycloid psychoses. Recently, in their scholarly review,

Jäger and coworkers stipulated the problematic reliability and validity of schizoaffective disorder and hinted at a fundamental reconsideration of the current diagnostic concepts of psychosis[20]. Similar suggestions were made by the research group of García-Andrade[21]. Therefore, the cycloid psychosis postulate needs to be revisited, particularly given its relevance for clinical practice.

The first set of operational criteria for cycloid psychoses was formulated by Perris and Brockington[22] and subsequently incorporated in the "Diagnostic Criteria for Functional Psychoses" of the World Psychiatric Association[23]. Starting with the ICD-10[24], the category acute polymorphic psychotic disorder without/with symptoms of schizophrenia (APP) is included that was derived from the Perris and Brockington (P&B) criteria. This category comprises, apart from cycloid psychosis, also the psychotic disorder bouffée délirante, used in France as a separate diagnostic category.

Clinical studies in patients with Leonhard's cycloid psychoses (LCP), using brain imaging[25] and event related potentials[26,27], have demonstrated that, in addition to variability in symptomatology, course, and prognosis, this class of psychoses is etiologically distinct from schizophrenia and bipolar affective disorders[28,29]. In rare cases of cycloid psychosis, disturbances in amino acid metabolism were observed[30,31]. Hereditary factors have been demonstrated to play a minor role[32,33], whereas environmental factors like maternal first-trimester gestational infection and obstetrical complications, seem to be of etiological importance[34,35]. Cycloid psychoses predominate in postpartum psychotic disorders[36,37].

The present study aims at delineating cycloid psychoses according to Leonhard's original descriptions and analyzes the diagnostic overlap with P&B as well as with ICD-10 and DSM-IV criteria.

Methods

Patient recruitment

All patients were recruited at the Vincent van Gogh Institute for Psychiatry, a large psychiatric teaching hospital in the southern part of The Netherlands with a catchment area of ~510.000 inhabitants. The recruitment period comprised 2.5 years (March 2008-September 2010).

Included were adult patients of both sexes (age range: 18-65 yrs) admitted for psychotic symptomatology that warranted treatment with psychotropics. Patients were included before the start or in the first week of treatment with psychotropics. In all cases, psychopharmacological treatment was performed according to the hospital standards by the responsible ward psychiatrist. Excluded were patients with proven genetic syndromes or intellectual disability. For this reason, a genetic work-up was performed by a registered clinical geneticist. Also excluded were patients with relevant somatic or neurologic diseases and females with postpartum psychopathology. All patients gave written informed consent following the Dutch medical ethical guidelines (CCMO registration number NL20469.097.07).

During the study period, a total of 194 patients were admitted for evaluation and treatment of psychotic symptoms of whom 100 were judged to be eligible for inclusion. Twenty patients refused to participate yielding a study group of 80 patients of whom 63 were available for follow-up assessment after at least 6 weeks (i.e., 63% of the initial selected group).

Diagnostic procedures and scoring instruments

Baseline diagnostic instruments comprised Comprehensive Assessment of Symptoms and History (CASH)[38], Positive and Negative Syndrome Scale (PANSS)[39], and Clinical Global Impression scales for Severity and Improvement (CGI-S/CGI-I)[40]. The CASH was specifically developed for research in the schizophrenia and affective spectrum conditions and is not uniquely connected to a classification system. PANSS and CGI were re-assessed at week 6. These assessments were performed by a well trained PhD-resident in psychiatry (NvdK).

Subsequently, classification was performed according to DSM-IV[19] and ICD-10[24] by NvdK and FvdH. Independently, the criteria for cycloid psychoses as advanced by Perris and Brockington[23] were applied to all subjects by a psychiatrist specifically trained in the diagnosis of cycloid psychosis (MS). In addition, using the symptom checklist of Leonhard[12,41] (Table 1), an internationally recognized psychiatrist (GS) delineated patients with LCP. Accordingly, a division into the three subtypes of cycloid psychosis was performed.

Analogous to a so called LEAD conference[42], in a final meeting with all investigators chaired by an independent experienced psychiatrist (WV), all available classificatory data were discussed to analyse the differential application of the various sets of criteria.

Statistics

For all statistic procedures, SPSS 14.0 software was used. Group differences were tested using the Student's t-test for continuous variables and Chi-square test for nominal variables. Cohen's kappa was used to test the concordance between the different categorical diagnostic groups. Significance was tested against $p < 0.05$.

Results

Total patient sample and symptomatic reduction after 6 weeks

The total group comprised 53 males and 27 females (mean age ± SD: 35 ± 11.5). Mean age at first episode and mean duration of psychotic disease were 27.4 ± 10.7 and 7.6 ± 7.9 years respectively. According to DSM-IV, 48 patients met the criteria for Schizophrenia. The remaining 32 patients fulfilled diagnostic criteria for Brief Psychotic Disorder: n = 10, Psychotic Disorder NOS: n = 7; Bipolar Disorder: n = 7; Schizoaffective Disorder: n = 5; Delusional Disorder: n = 2; and Schizotypal Disorder: n = 1.

Patients were treated with classical/first generation (n = 27) and atypical/second generation (n = 61) antipsychotics, either as monotherapy (n = 72) or in combination (n = 8). After six weeks of treatment, scores on the PANSS total, positive, negative and global scales decreased from 86 to 69 (20%), 23 to 17 (26%), 20 to 17 (15%) and 43 to 35 (19%) respectively. The CGI-S improved from 4.5 to 3.4 (23%). All comparisons were statistically significant ($p < 0.001$).

Diagnosis of cycloid psychoses according to P&B criteria and Leonhard

Concerning cycloid psychosis according to P&B, 14 patients (18%) met the criteria. According to Leonhard's descriptions, in 12

Table 1
Symptom checklist for cycloid psychosis (translated by Pfuhlmann [adapted from Leonhard, 1990])

Original checklist symptom description	Translation
1. Ängstliche Stimmung	Anxious mood
2. Angstvorstellungen (Bedrohungsideen, ängstliche Beziehungsideen)	Anxious beliefs and delusions (ideas of threat, anxious ideas of (self-) reference)
3. Ängstlich hypochondrische Ideen	Anxious hypochondriacal ideas
4. Pathetisch-euphorische Stimmung	Ecstatic elation
5. Beglückungsideen (altruistischer Charakter)	Altruistic ideas of happiness
6. Angst und Euphorie im raschen Wechsel	Rapidly changing anxiety and euphoria
7. Selbstopferungsideen	Ideas of self-sacrifice
8. Affektkongruente optische Sinnestäuschungen (aus Angst oder Ekstase)	Mood congruent optical illusions or hallucinations (driven by anxiety or ecstasy)
9. Affektkongruente Stimmen (aus Angst oder Ekstase heraus)	Mood congruent voices (driven by anxiety or ecstasy)
10. Rededrang mit Inköhärenz der Themenwahl	Pressure of speech with incoherence of thematic choice
11. Beziehungsideen mit Ratlosigkeit und Hemmung	Ideas of reference with perplexity and thought inhibition
12. Bedeutungsideen bei Ratlosigkeit	Ideas of significance in association with perplexity
13. Stimmen aus Ratlosigkeit	Voices in association with perplexity
14. Denkhemmung	Inhibition of thought
15. Ratloser Stupor	Confused stupor
16. Flüchtige Personenverkennungen	Fleeting misrecognition of persons
17. Psychomotorische Erregung mit vermehrter Ausdrucks- u. Reaktivmotorik	Psychomotor excitement with increased expressive and reactive movements
18. Starke Ablenkbarkeit durch äußere Gegebenheiten	Strong distractability by environmental stimuli
19. Sinnlose (“leerlaufende”) motorische Aktivität (keine Vielgeschäftigkeit!)	Senseless motor activity (not general overactiveness!)
20. Sinnlose motorische Sprachentäusserungen (Schreien, Johlen, Wortfetzen)	Senseless motor speech expressions (screaming, yelling, syllables)
21. Psychomotorische Verlangsamung	Psychomotor slowing
22. Stupor mit starrer Motorik	Stupor with stiff posture

Note:
Symptom 1-9: *Anxiety-happiness psychosis*
Symptom 10-16: *Confusion psychosis (inhibited/excited pole)*
Symptom 17-22: *Motility psychosis (akinetic/hyperkinetic pole)*

patients a cycloid psychosis was present reflecting a prevalence of 15%. Leonhard's cycloid psychoses could be further specified as anxiety-happiness psychosis (n = 5), confusion psychosis (n = 3), and motility psychosis (n = 4). Brief case vignettes are depicted in Table 2.

Of the 14 patients with P&B cycloid psychosis, 9 also accorded with Leonhard's descriptions (Table 2: no. 1-4, 6-9, and 11).

In Table 3, the main characteristics of the non-cycloid (n = 68) and LCP (n = 12) patient groups with their corresponding DSM-IV, ICD-10 and P&B diagnoses are presented. As can be inferred, the LCP subgroup has a higher age at onset of both psychosis and general psychiatric symptoms. LCP as well as non-CP groups show diagnostic heterogeneity, albeit that a diagnosis of schizophrenia, according to ICD and DSM, is exclusively made in the non-CP group. In the LCP group,

Table 2
Core symptomatology in patients with cycloid psychosis (Leonhard, 2003)

No.	Sex/age	Signs and symptoms	Leonhard diagnosis
1	♀, 27	Fear of death, suspicion, suspicious anxiety, mood congruent imperative voices with aggressive behaviour towards mother	Anxiety psychosis
2	♂, 39	Mutism, stupor, no spontaneous action, bad self-care, severe akinetic symptoms, reduced thinking	Motility psychosis, akinetic pole
3	♀, 35	Moving and removing things, elated mood, non-goal directed psychomotor activity, sleep disturbances, paranoid ideation, angry outbursts	Motility psychosis, hyperkinetic pole
4	♂, 36	Pananxiety, religious delusions, anxious stupor, perseveration, verbigeration	Anxiety psychosis
5	♀, 53	Anxiety and dysphoria, behaviour driven by suspicion, mood congruent delusions of guilt, mood swings, transient auditory, tactile and olfactory hallucinations	Anxiety psychosis
6	♂, 39	Illogical thinking, higher awareness of meaning, visual misinterpretations, delusions of reference	Confusion psychosis
7	♂, 36	Delusion of grandiosity, pressure of speech, poor concentration, visual misinterpretations, psychomotor agitation, chaotic behaviour	Confusion psychosis
8	♂, 47	Anxiety, religious delusions, pressure of speech, emotionally driven behaviour, illogical thinking	Anxiety-happiness psychosis
9	♀, 33	Chaotic thinking, auditory hallucinations, mood swings, inadequate behaviour	Confusion psychosis (inhibited pole)
10	♀, 61	Anxiety-driven behaviour, catastrophic thinking, illogical speech, delusions of persecution and control, mood swings	Anxiety-happiness psychosis
11	♀, 46	Chaotic and inhibited, confusion, ritualistic behaviour, perseveration, disorganised speech, paranoia	Motility psychosis
12	♀, 56	Psychomotor agitation, sleep disturbances, delusions of reference and grandiosity, chaotic thinking	Motility psychosis

Table 3
Clinical characteristics of the sample (n = 80); Leonhard cycloid psychosis (LCP) versus non-cycloid psychosis (Non-CP)

	LCP (n = 12)	Non-CP (n = 68)
Demographics		
Male/female ratio	5/7	48/20
Age, years (mean ±SD)*	42.8 (±10.5)	33.1 (±11.2)
Age at onset general symptoms (mean ±SD)**	31.8 (±12.6)	20.9 (±10.8)
Age at onset psychosis (mean ±SD)**	38.2 (±11.2)	25.5 (±9.5)
Number of episodes (mean ±SD)	2.2 (±1.5)	2.9 (±2.8)
PANSS total score baseline	77	88
PANSS total score after 6 weeks**	55	72
DSM-IV diagnoses		
– Schizophrenia	0	48
– Schizoaffective disorder	2	3
– Bipolar disorder	2	5
– Brief psychotic disorder	7	3
– Psychotic disorder NOS	1	6
– Delusional disorder	0	2
– Schizotypal disorder	0	1
ICD-10 diagnoses		
– Schizophrenia	0	50
– Schizoaffective disorder	4	2
– Bipolar disorder	1	5
– Acute and transient psychotic disorder[a]	7 (4)	4 (3)
– Psychotic disorder NOS	0	3
– Persistent delusional disorder	0	3
– Schizotypal disorder	0	1
Meeting Perris & Brockington criteria for cycloid psychosis	9	5
Antipsychotic treatment		
– Classical agents	2	17
– Atypical agents	10	43
– Combination of antipsychotic agents	0	8

* Difference between LCP and Non-CP cases, $p<0.05$.

** Difference between LCP and Non-CP cases, $p<0.01$.

[a] Any F23 diagnosis, including acute schizophrenia-like disorder. The numbers of patients meeting criteria for Acute Polymorphic Psychosis (APP; F23.0/F23.1) are inserted between brackets.

diagnoses of DSM-IV Brief Psychotic Disorder or ICD-10 Acute and Transient Psychotic Disorder are represented more often.

With respect to severity of symptomatology as assessed with the PANSS, total scores at baseline did not reveal differences between the two groups. After 6 weeks of treatment with antipsychotics in a naturalistic setting, however, the symptomatic decrease was more pronounced in the cycloid group ($p < 0.01$).

Psychopathology

Detailed analysis of the individual symptomatology of the LCP patients (n = 12) and those who met the P&B criteria (n = 14), revealed that the seven symptoms "ecstatic elation", "altruistic ideas of happiness", "rapidly changing anxiety and euphoria", "pressure of speech with incoherence of thematic choice", "confused stupor", "psychomotor excitement with increased expressive and reactive movements" and "stupor with stiff posture" (Table 1, symptom checklist items 4-6, 10, 15, 17 and 22) are most prevalent in both or either group of patients, indicating that bipolarity of mood, thought and locomotion, frequently occurring also intraphasic, are key symptoms of cycloid psychosis. Moreover, these key symptoms are virtually identical to those from the extreme poles as originally described by Leonhard.

Table 4 illustrates the symptom profile of the 12 patients with LCP as compared to the group of non-cycloid psychosis (n = 68) by applying the P&B criteria. Whereas delusions and hallucinations are present in most of the patients in both groups, the atypical symptoms (perplexity, ecstatic feelings, motility disorders and pananxiety) are overrepresented in the LCP subgroup.

Table 4
Frequency distribution of Perris & Brockington criteria in Leonhard cycloid psychosis (LCP) and non-cycloid psychosis (Non-CP)

	LCP (n = 12)		Non-CP (n = 68)		p
Perris & Brockington criteria	*n*	*%*	*n*	*%*	χ^2
Perplexity	11	91.7	12	17.6	<0.001
Ecstatic feelings	6	50.0	14	20.6	0.030
Akinesia or hyperkinesia	8	66.7	15	22.1	0.002
Mood-incongruent delusions	12	100	64	94.1	n.s.
Hallucinations	12	100	56	82.4	n.s.
Pananxiety	9	75.0	20	29.4	0.002
Concern with death	4	33.3	10	14.7	n.s.
Mood swings	6	50.0	20	29.4	n.s.
Acute onset	12	100	8	11.8	<0.001

Cycloid psychosis: representation in ICD/DSM and concordance rates

Concordance rates were calculated for LCP (n = 12) and the most frequent DSM-IV and ICD-10 diagnoses in this group (see: Table 3). Between LCP on the one hand and ICD-APP and DSM-BPD on the other hand a concordance rate of 0.58 and 0.35 (both $p \leq 0.001$) was present respectively (Figure 1a,b). A concordance rate of 0.63 ($p < 0.001$) was calculated between LCP diagnosis according to Leonhard's symptom checklist and P&B criteria whereas a rate of 0.38 ($p < 0.001$) was found between LCP and ICD schizoaffective disorder (SAD) (Figure 1c,d). The concordance between LCP and DSM-SAD did not reach statistical significance.

Discussion

In this observational study with a group of patients admitted for psychotic disorders, the presence of cycloid psychoses according to both Leonhard's descriptions and the criteria as established by Perris and Brockington, was investigated. A prevalence rate of 15% was found for Leonhard's cycloid psychoses. It appeared that cycloid psychosis can also be diagnosed according to the P&B criteria, whereas application of Leonhard's descriptions additionally provides differentiation in the three subtypes.

The highest concordance was calculated between LCP and P&B, whereas lower concordance rates emerged between LCP and the different ICD-10 (APP and SAD) and DSM-IV (BPD) categories (Figure 1a-d).

With respect to the prevalence of cycloid psychosis, the here observed frequency of 15% is in accordance with that reported by other investigators (8-24%)[14,43-46]. The prevalence from this study may, however, be biased negatively since female patients with postpartum psychopathology were a priori excluded and the sample size was limited due to the strict inclusion criteria as defined by the Dutch ethical rules for genetic work-up and for patients admitted under a legal act. Still, the overrepresentation of female patients in our cycloid group is in line with the results from other studies[11,14,47].

Since the majority of the patients who were diagnosed as LCP were classified as ICD-10 APP or DSM-IV BPD, the concordance rates between these categories are most relevant (Figure 1a,b). Albeit that the observed values are higher than those reported by Pillmann and coworkers[47] with ICD-10 Acute and Transient Psychotic Disorders (including APP) of 0.36 and by Van der Heijden and coworkers[46] with 0.24 for BPD and 0.31 for APP, it has to be underlined that in the latter studies, patients were classified according to P&B criteria only. This suggests that the criteria for DSM-BPD and ICD-APP do neither cover sufficiently the descriptions by Leonhard nor the P&B criteria and that particularly Leonhard's symptom checklist is most promising for clinical practice. It has to be stressed, however, that this study is the first to systematically investigate this checklist on its relation to classification systems and thus needs further scientific evaluation.

The observed discrepancies in overlap between LCP and both ICD-APP and DSM-BPD may be explained by the duration criterion. In DSM-IV as well as ICD-10, a maximum duration of 1 to 3 months is required which excludes a priori the cycloid psychoses that are characterized by highly variable duration and frequently relapsing course[18,35,48-51].

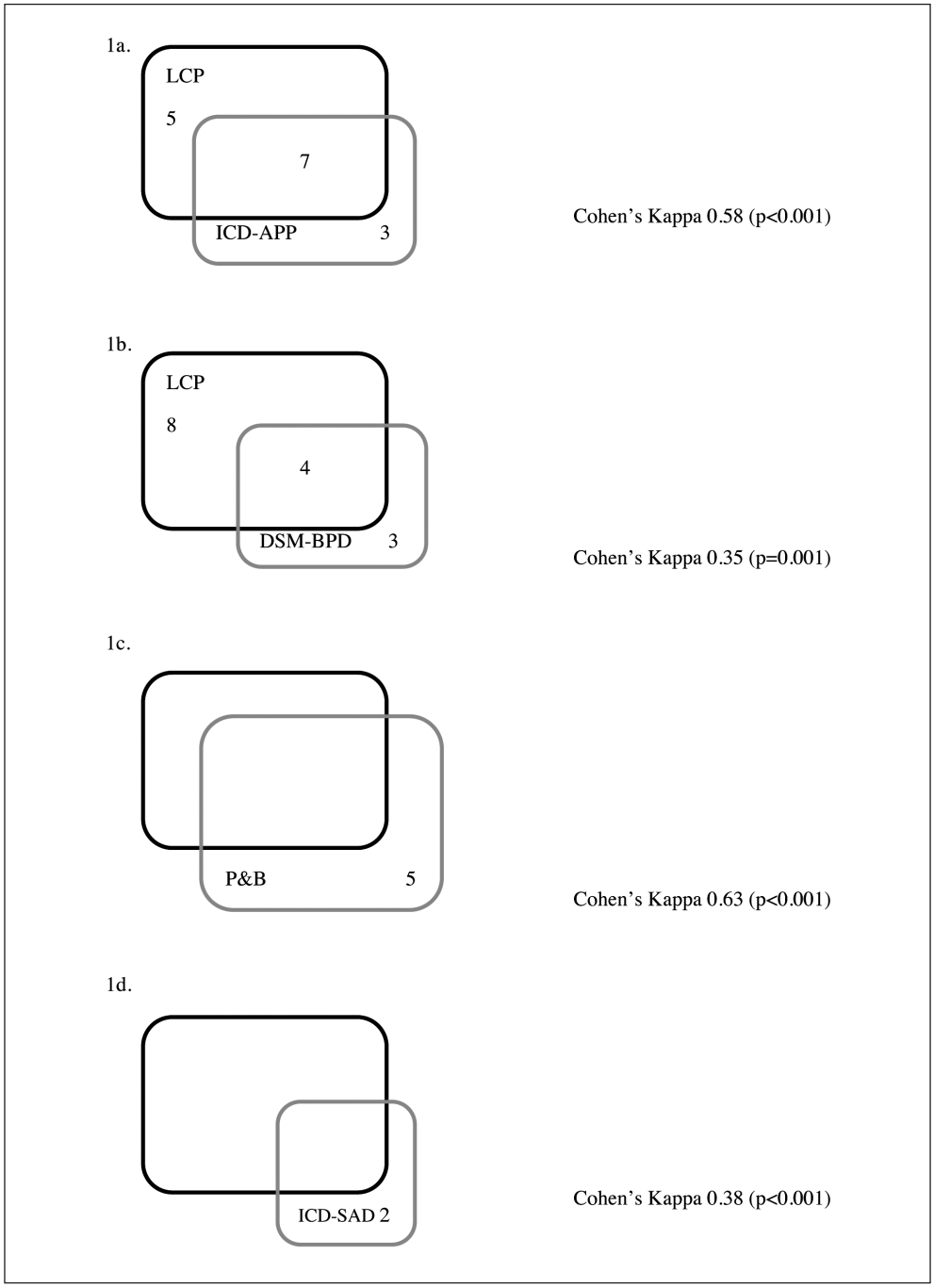

Figure 1a-1d. Concordance rates. Concordance between Leonhard's cycloid psychosis (LCP, n = 12) and a: DSM-IV Brief Psychotic Disorder (DSM-BPD, n = 10), b: ICD-10 acute polymorphic psychotic disorder (APP, n = 7), c: Perris and Brockington criteria (P&B, n = 14) and d: ICD-10 schizoaffective disorder (ICD-SAD, n = 6).

As can be inferred from Figure 1c, the concordance rate between LCP and P&B is also rather moderate which may be due to the onset and age criteria, in that the onset criterion in P&B comprises a time interval of hours to days, while in LCP this is not quantified. Moreover, in P&B the criterion age is restricted to the range 15-50 years, while according to the original monograph, LCP does not comprise any age limitation. That three LCP cases are discordant with P&B cycloid psychosis, is explained by the age criterion (> 50 years old at first presentation; n = 2) or the required number of symptoms (≥ 4; n = 1). With respect to the overlap between LCP and SAD, it has to be stressed that this finding is rather irrelevant since the SAD as included in the ICD-10 and DSM-IV cannot be compared with the acute schizoaffective psychosis as originally described by Kasanin[4] and is not clearly demarcated from schizophrenia and affective disorders[20].

As demonstrated in the present study, the three subtypes of cycloid psychosis can clearly be discriminated from other psychotic disorders by their pronounced symptomatological presentation and intraphasic bipolarity (Table 1). Key features of their core syndromes include perplexity, pananxiety, motor disturbances, mood swings and transient hallucinatory experiences of any kind.

Interestingly, in the cycloid psychosis group a higher symptom reduction was found after 6 weeks on antipsychotics from various classes. Although not the main target of the present investigation, the pharmacological maintenance treatment of cycloid psychoses is suggested to be primarily with mood stabilizers[17,52] whereas in the acute phase atypical antipsychotics may be beneficial[18]. Generally, these psychoses have a good prognosis[15,35,48,53] and their diagnostic stability is high[54,55].

In conclusion, the results demonstrate that the concept of cycloid psychosis is still clinically useful and valid. It would be therefore wise to include a separate group of nonaffective acute psychoses in the future editions of current international classification systems. Such a proposal was recently also formulated by Nugent and coworkers[56]. Given the rather high prevalence of this kind of psychosis, further clinical studies with differential assessment methods such as Leonhard's symptom checklist are warranted and should particularly focus on treatment strategies and long term outcome.

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