Anxiety-happiness psychosis, a cycloid psychosis

J. R. FOUCHERb,c, V. BENNOUMA-GREENEb, F. BERNAa,b,c, B. PFHLMAND,
G. STÖBERD

aINSERM U666 – Physiopathologie Clinique et Expérimentale de la Schizophrénie,
Strasbourg, France
bHUS, Hôpitaux Universitaires de Strasbourg, Strasbourg, France
cUdS, Université de Strasbourg, Strasbourg, France
Department of Psychiatry and Psychotherapy, University of Wuerzburg, Wuerzburg, Germany

Introduction

“Angst-Glücks-Psychose” has several translations in the literature: anxiety-happiness psychosis (AHP), anxiety-elation or anxiety-bliss psychosis. AHP is one of the 3 phenotypes of the cycloid psychosis (CP) as defined by the Wernicke-Kleist-Leonhard (WKL) school [26]. CP are bipolar psychoses in that they manifest in two opposite clinical pictures that may alternate from one episode to the next or during the same episode (mixed state). AHP as all CP has a purely relapsing-remitting course without accumulation of other symptoms between episodes; this can be opposed to non-systematic schizophrenias that come with an initial episodic course as well, but where residual symptoms, e.g. lameness, indifference of affect up to flatness or blunting, loss of drive, but also other symptoms such as paranoia, hallucination, language disorders, increase at each remission. Psychosis or emotional disturbance could either appear as prevalent to a ICD/DSM formatted mind, but this symptomatology is too rough to distinguish them from non-systematic schizophrenias.

2. History

Acute and purely episodic psychoses have been distinguished by Valentin Magnan from Paris who named them “bouffée délirante aiguë des dégénérés” [24]. At about the same time, but independently, Theodore Meynert from Vienna described the “Amentia”, a remitting psychosis with a confusional component [31].

According to Kraepelin, because of their good prognosis, most of these forms were probably included in the manic-depressive illness. Nevertheless Kraepelin appeared uncertain how the Amentia should be classified [22].

Bleuler did not experience such difficulties as he abandoned the evolutional principle for a purely psychopathological principle (“der Spaltung”). The acute remitting psychoses were part of his “schizophrenias” [8; 9].

Schröder is the one who imported the French concept of “Bouffée Déliante Aiguë” in Germany and showed its differences compared to manic-depressive illness. He also quoted the term of “cycloid psychosis” [42; 43]. But it was the WKL school that
refined their clinical manifestations in a way that allows to differentiate them from the ones with a more unfavourable outcome [26]. The latter is what differentiates the most between the concepts of bouffée délirante and CP. In short, whereas the bouffée délirante is a diagnosis of an episode, a CP is a life long diagnosis. That for, CP have to be differentiated from unsystematic schizophrenias which are psychoses of unfavourable course. These can closely look like CP during the first or the second psychotic break (see table 1). As such, the clinical picture allows 80% of the patients to be correctly classified upon their first psychotic break (10 years follow up) (Pfuhlmann et al. in preparation).

Table 1. Cycloid psychoses and their differential diagnosis of unsystematic schizophrenias

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<thead>
<tr>
<th>Psychic function</th>
<th>Cycloid psychosis</th>
<th>Unsystematic schizophrenia</th>
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<tr>
<td>Emotion</td>
<td>Anxiety-hapiness psychosis</td>
<td>Affective paraphrenia</td>
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<tr>
<td>Thought</td>
<td>Confusional psychosis</td>
<td>Cataphasia</td>
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<tr>
<td>Psycho-motility</td>
<td>Motor psychosis</td>
<td>Periodic catatonia</td>
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2. Clinical picture

Leonhard classifies the phenotypes of CP according to the most impaired psychic function: emotion, thought, psychomotility. In AHP, the impairment predominates on the emotional sphere with the two polarities of anxiety or happiness on the foreground [26]. Although thought and psychomotility might also be affected, this is secondary to the emotional disturbance. Delusions, hallucinations or disorganization are frequently observed and sometimes intense, but remain always closely related to the affectivity. In developed countries the anxiety pole may be more frequent than the happiness one. However, the mood is most often fluctuant and commonly mood switches of short duration to the opposite pole can be observed (minutes to hours). The episode has an acute (< 48 h) or sub-acute (< 2 weeks) beginning in the majority (2/3) of cases. Prodromal symptoms can be observed, e.g. half of the patients report a sleep deficit in the 50 days prior to the beginning of the episode.

2.1. Anxiety psychosis

The ambient mood is massive anxiety and its intensity is correlated with a higher diagnostic probability. The patient’s mimic and behaviour is supported by anxiety. Its expression is variable: the patient may cry, complain, shout and actively avoid any effort to comfort him. He can be very excited and may attempt to escape or even fight if he feels cornered. Conversely he may remain still, in a stiff posture (anxious stupor), with his eye movement and facial expression alone indicating anxiousness. Anxiety characteristically is accompanied by distrust, self references and mood congruent delusional ideas. The patient's ideas are centered on fear, of for example dying, being killed, tortured, or that this may occur to one of his relatives. However there is no specific persecutor. Occasionally the patient has the impression that the end of the world is near or that another devastating disaster affecting human mankind is about to occur. Although these ideas emerge without any precipitating factor, they are
consolidated by external events. Frequently, the patient reports verbal or visual hallucinations or pseudo-hallucinations in line with these ideas and feelings. In religious persons they are referred to the Devil, coming from the hell. It is not always clear whether the patient reports an hallucinatory perception or a delusional interpretation. Hypochondriac complaints can also be observed: the patient feels heating or tingling sensations, or senses his body shake (coesthestic hallucinations). Generally, the clinical expression fluctuates hours by hours, i.e. polymorphic characteristic.

2.2. Happiness psychosis

The patient describes an intense feeling of happiness, an oceanic feeling of well-being, a feeling of ecstasy. The behavioral expression varies from exaltation to immobility in pathetical praying posture together with an enraptured mimic, the patient being disconnected from reality. The patient expresses ideas of grandeur with commonly a religious flavor. He feels he is being called for a mission that has been given to him by God. The ideas of grandeur-unlike those found in mania or affective paraphrenia are mainly altruistic. In fact, the patient often does not attach much importance to his own person; indeed the patient is the messenger, the messias, not God himself and is only the means God chose to deliver a message. He must deliver a message of peace, freedom or happiness to this world and make others happy, giving money to the poor. In women, the idea of grandeur is sometimes carried over onto her children (celebrity, fortune …). The patient may feel ecstatic, awaiting a great event to come soon like the time for universal salvation or for the crack of doom, if anxiety plays a role too. Hallucinations or pseudo-hallucinations are mood congruent and typically include divine inspirations (phonemes) or divine visions. They can develop together with affect-triggered misinterpretations of external events.

2.3. Rapid switch between the two poles and incompleteness of poles

Affect in AHP is not only excessive, but also fluctuating. Its intensity and even its polarity may change very quickly. Changes can sometimes be triggered by external events such as ecstatic feelings triggered by the visit of a priest. Such rapid changes (ultradien) are considered by the DSM as a mixed state. Rapid oscillations from one pole to another can result in the expression of apparently contradictory ideas or a mix of ideas from the two poles, the most classical being the idea of self-sacrifice for the sake of mankind. Otherwise the patient may express the idea of one pole whilst being already in the other one and this appears as inappropriate affect.

Besides these changes, the poles are also in some cases incomplete. This means that symptoms from the psychomotor or thought functions do not always go with the emotion, e.g. hypo-activity and slow thought together with happiness. This is the Kraepelin-Weygand concept or mixed state.

3. Evolution

Before the neuroleptic era, an episode would spontaneously remit in 3.9 months on average (range from a few days to 2 years) [26]. The remission is complete: the patient recovers his previous state and there is full insight into the psychotic incident. Any lack of insight about the pathological nature of the episode and its symptoms should lead to
a diagnostic reevaluation. During long-term, recurrence of episodes is the rule with an average of 1 episode every 2 to 3 years [26]; Pfuhlmann et al. in preparation). Their frequency does not appear to increase with time and may even decrease.

Many patients have an accentuated temperament with strong and sudden emotional fluctuations [26; 38]. Frequently psychoanalysts diagnose a “psychotic personality structure” that should be understood in the psychoanalytic sense. These personality or temperamental peculiarities in those subjects developing endogenous psychoses have been noticed since the description of Valentin Magnan who interpreted them as a stigma of degenerescence [24]. But these traits remain stable in time whatever the number of episodes.

Finally, these patients frequently have depression-like episodes, mostly of the post-psychotic kind. Their occurrence are part of the genuine course of the disease but may be favored by an excess of neuroleptic doses. A minima, patients frequently describe a depressive or irritated mood, or slight cognitive difficulties, e.g. concentration, after the episode itself, lasting a month to a year before recovering their initial level of functioning.

Table 2. Core features of anxiety-happiness psychosis

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<td>&gt; Severe anxiety with distrust and idea of reference</td>
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<td>&gt; Ideas of threat or persecution</td>
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<tr>
<td>&gt; Anxiety with paranoid features and/or mood congruent sensory illusion or hallucination</td>
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<td>&gt; Anxiety with hypochondriac somatic sensations</td>
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<th>Happiness psychosis</th>
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<tr>
<td>&gt; Ecstatic mood and feeling of happiness with illusionary or hallucinatory experiences</td>
</tr>
<tr>
<td>&gt; Ecstatic ideas with altruistic components (religious, social or political tasks)</td>
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<tr>
<td>&gt; Waves of bliss with ideas of being called, elevated to a divine level or inspired by God.</td>
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4. Differential diagnosis

Within the 35 major phenotypes, differential diagnosis could be numerous, but 3 most peculiarly deserve to be discussed [26].

4.1. Affective paraphrenia

This diagnose frequent as it accounts for up to 10% of endogenous psychoses, i.e. ranging from affective disorders to schizophrenias. It belongs to the family of unsystematic schizophrenias which generally run a relapsing-progressive course, i.e. episodes with more and more residual symptoms in the interval. As such, the differential diagnosis remains difficult in the beginning. However subtle differences allow to correctly classify AHP even in the first break: the illogical quality of the delusional ideas, the identification of a persecutor, the frequent description of anger and distrust with aggressive outbursts, the egoistic quality of ideas of grandeur. In affective paraphrenia psychotic symptoms will at least partially go on to persist during the
interval. Unfortunately a deficit is the rule after 10–20 years of evolution, i.e. flattening of affect outside of the chronic delusional system and hallucinations, fantastic ideas, loss of motivation and spontaneity.

Interestingly enough, in a recent functional connectivity study, affective paraphrenia and CP patients were different (Foucher et al. in preparation). Relative to controls, both shared a common core of disconnected regions: the anterior cingulate cortex, the internal temporal regions and the temporal pole, the latter being specific to humans. But a double dissociation could be shown between these two clinical pictures:

• The temporal regions were hyper-connected in CP relative to both controls and affective paraphrenia,
• Affective paraphrenia had a larger disconnected network encompassing the orbito-frontal regions and the posterior cingulate cortex in comparison to both controls and CP.

4.2. Process phase of systematic schizophrenias

The WKL school grouped under this label 53 diagnoses (16 simple forms + 37 combinations of the previous ones). Systematic schizophrenias account for 20% of endogenous psychoses at a university department. They begin by an initial process phase followed by a distinctive stable symptomatic state. The “schizophrenic course” recently popularized by Stanley Lieberman is very much alike the one of WKL systematic schizophrenias. Some symptoms of the process phase can be mistaken for anxiety psychosis at the very beginning: chronic irritability, affective alteration, transient delusions, mood swings etc... But other symptoms that point to a specific subform of systematic schizophrenias and occur already early in the course of the illness should help to correct the diagnosis and therefore the prognosis.

4.3. Manic-depressive psychosis (MDP)

WKL’s definition for MDP is much more refined than the initial, classical concept and even the one of bipolar disorders, although it constitutes its precursor. However it remains the most frequent of endogenous psychoses accounting for about 20% of them. Regarding cross-sectional symptomatology MDP characteristically does not show the specific disturbance of affect in the sense of an intensive anxiety associated with ideas of reference, persecution or thread. Threatening phonemes are also not present in MDP which in contrast can show depressive psychotic symptoms like ideas of guilt or punishment due to supposed sins. In general, MDP has a much larger spectrum of symptomatic expression which should even appear during the same episode as the disorder is proteiform. Although the distinction is of limited interest at prognostic levels, the etiology appears very different: mostly hereditary for MDP, mostly acquired during pregnancy and birth for AHP.

We could have also developed the differential diagnosis of AHP with the two other CPs (confusion psychosis and motility psychosis). Indeed there is some symptomatic overlap especially during the acute phase. The differences become clearer as the patient gets better. However there are no prognostic, therapeutic or etio-physiopathological differences that have been demonstrated today between them.
5. Relations of AHP with ICD-10 and DSM4 diagnostics

As a whole CP tends to cover the spectra that ranges from affective disorder to schizophrenia. The ICD/DSM diagnoses however frequently change from one episode to the other.

The category of acute and transient psychosis from the ICD-10 was designed to capture CPs [30; 35]. But not only does it miss most of them essentially because of its rather arbitrary time criteria, i.e. mostly < 1 month whereas a typical CP episode has an average 3 months duration, but it also includes other acute psychoses than CP because of imprecisely defined symptoms, e.g. the above mentioned differential diagnoses, except MDP. However if the category is even more refined and limited to the acute and transient psychosis with polymorphic features, i.e. quickly changing clinical symptoms, the Halle study suggests that most of the patients might also fit with the diagnosis of CP [30; 41]. Unfortunately the reverse is not true: most of CP do not fit with the diagnosis of acute and transient psychosis with polymorphic features.

The situation is even worse with the DSM as CPs contribute to the good prognosis of brief psychotic episode and schizophreniform disorder if the later is understood as a “good prognosis schizophrenia” as it was designed to be, and not as a waiting diagnosis as many use it today [4]. However both miss some CP and melt them with other forms.

6. Treatment

Unfortunately this is the least developed aspect of the WKL classification. Most of the following mentioned recommendations are at best supported by retrospective studies of CP. There is no specific data for AHP.

6.1. Acute episode (acute and stabilization phase)

AHP shares with most of the bipolar forms (CP, MDP, non-systematic schizophrenias) a good response to antipsychotics [5; 32; 34; 37]. However these patients might be especially sensitive to their side effects. Thus atypicals should be preferred.

Benzodiazepines are often useful in addition to antipsychotics in cases of severe anxiety and agitation.

All authors reported the very good response of CP to electro-convulsive therapy with rapid and complete remission [10; 12; 21; 27; 28; 37; 44]. The problem is its limited time duration since a psychotic episode lasting 3 months on average requires a stabilization treatment that lasts long enough.

Although mood stabilizers are probably efficacious there is no data for the acute phase.

6.2. Prevention (stable phase)

As previously mentioned, the prognosis of CP is purely related to the recurrences. There is no symptomatic progression or residual state to prevent.

Above all prevention relies on the eviction of precipitating factors when possible: cannabis consumption (THC), stress, sleep deficit and hormonal factors (see later). Medication should be considered with the patient taking into account the frequency of recurrence and the long term tolerance to the adverse effect of medication.
Regarding antipsychotics, the WKL school is not entirely in line with the current guidelines. Leonhard preferred not to maintain patients under these medications because the anhedonic-aboulia effect makes them look like residual schizophrenia with deficit symptoms [26]. Moreover some clinical observations suggest that long duration of antipsychotic treatment makes these patients especially vulnerable to relapse upon the withdrawal of medication, a picture that has been described by Guy Chouinard as neuroleptic supersensitivity psychosis [1; 11; 33]. Thus medication is very slowly tapered off after remission (1 – 2 years). Although this fits with the guidelines for the first episode, consensus does not advise this after the second psychotic break (maintenance for 5 years to life). However to date, there is no study ascertaining the preventive effect of neuroleptics on this diagnostic entity. It is important to remind that despite a relapsing-remitting course, some require clozapine to be cured or because of a too large amount of recurrences.

The WKL school advises to treat these patients as purely phasic or forms, i.e. like bipolar disorders. We only have evidence for a protective effect of lithium and by extension of the other mood stabilizers. In a recent retrospective study, CP patients that could be maintained under lithium had a better psychosocial outcome than patients under antiepileptic drugs although this difference might be due to the naturalistic nature of this study (Pfuhlmann et al. in preparation). There were no significant differences in the number of recurrences between lithium and antiepileptic drugs, but the groups were small and thus the study might lack power.

7. **Etiological and physio-pathological research**

The WKL classification system is devoted for such studies. We have no specific data for AHP but only results for the CP group as a whole. These will be summarized according to the framework of a vulnerability-stress model that peculiarly fits to CP.

7.1 **Vulnerability factors**

CP have a very low hereditary burden, not significantly different from controls, but significantly different from MDP on one side and non-systematic schizophrenia on the other [20; 29; 39]. E.g. there is a significant difference for age-corrected lifetime morbidity risk for endogenous psychoses in first degree relatives: 30% of WKL’s MDP relatives, 20 to 25% of non-systematic schizophrenias’ relatives (cataphasia and periodic catatonia) and 10% for CP relatives (5% for relatives of controls from the general population). Interestingly most relatives of the two former groups do have homotypic forms which is less likely so for CP. Corresponding results regarding a high heritability in MDP and unsystematic schizophrenias and a low heritability in CP came from a twin study [17].

Conversely problems during pregnancy and birth are more likely to occur in mothers of CP patients compared to mothers of patients with non-systematic schizophrenias [25]. A seasonal birth effect is also significantly larger in the former than the latter group, which is interpreted as possibly related to more frequent viral infections during pregnancy in mothers of CP patients [16; 45].

Larger ventricles and brain anomalies on CT and MR scan also gave further evidence for a precocious lesion in CP compared to non-systematic schizophrenia [7; 13; 15; 46].
Precipitating factors

A significant psychosocial stress is frequently described in the weeks preceding the psychotic break: divorce or separation (22%), difficulties at work (24%), and an unfavorable social context (27%) [6; 37].

A lack of sleep is reported in the 50 days before the relapse by a half of the patients and some patients describe the absence of recurrence when preventively treating it [6; 12; 18; 19].

Cannabis might be one of the lead precipitating factors to date [12]. Its weaning helps to reduce the frequency of episodes. Some cannabis-induced psychoses may belong to the CP group [36]. Psychotic patients frequently use it as an anxiety reduction strategy and generally do not perceive the rebound of anxiety or even psychosis that occurs some hours later [47].

Finally, CP are very sensitive to the hormonal status in women: 90% of the episodes begin in the last half of the cycle [2; 3] and 45 to 62% of post-partum psychosis are CP, with a relapsing risk of 12% per birth [23; 40].

Although it is too early to conclude about the physiopathology of CP, the disconnectivity hypothesis may fit with the above mentioned physiological and etiological correlate: a reduced number of synapses from the beginning, further aggravated by stress, lack of sleep, hormonal status or drugs that are all known to decrease connectivity at least functionally [14].

Conclusion

Evidences are strong for distinguishing AHP and the other CP from the schizophrenias on one side and MDP on the other, e.g. course and etiology. However most knowledge we have are about CP as a whole. Further developments should consider AHP as a specific entity and investigate its physiopathology and therapeutic specificities.

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