Single Episode of Major Depressive Disorder

First Episode of Recurrent Mood Disorder or Distinct Subtype of Late-onset Depression?

Giovanni B. Cassano¹, Hagop S. Akiskal², Mario Savino¹, Adalgisa Soriani¹, Laura Musetti¹, and Giulio Perugi¹

¹II Psychiatric Clinic, Institute of Clinical Psychiatry, University of Pisa, Italy
²University of California at San Diego, San Diego, California, USA

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Summary. Of 687 consecutive inpatients and outpatients with primary major depressive illness, 213 (31%) were categorized as single episode (SE) by DSM-III-R criteria. Systematic evaluation of familial, sociodemographic, temperamental and symptomatological characteristics permitted the nearly equal division of SE into two categories: a. early-onset (< 45 years) “first episode” superimposed on either depressive or hyperthymic temperaments (against a bipolar and unipolar familial background), more severe depression, higher rates of suicide attempts, greater anxiety-somatization and psychotic tendencies, and with the potential for recurrence; b. late-onset (≥ 45 years) isolated episode (against an unipolar familial background) with greater life stressors, pursuing a protracted course with less likelihood of recurrence. In most other respects, early-onset SE was intermediate between recurrent major depression and late-onset SE. The implications of these findings for the now largely abandoned category of “involutional melancholia” are discussed.

Key words: Late-onset depression – Single-episode depression – Hyperthymic and depressive temperaments

Introduction

A first major depressive episode (MDE) that does not recur during follow-up has been reported to be relatively uncommon (Kinkelin 1954; Stenstedt 1959, Astrup et al. 1959, Angst 1978; Akiskal et al. 1978, Zis et al. 1980). Thus, at the first episode, the clinician is expected to assess which disorder (recurrent unipolar or bipolar) the depressive episode will ultimately belong to. However, a substantial minority, as many as one out of three depressives (Kinkelin 1954, Perris 1968) do not progress beyond an isolated single episode (SE). According to Akiskal and McKinney (1973), these isolated depressive episodes could be determined by the action of multiple environmental factors superimposed on a predisposing ground, rather than strong genetic factors which appear important for bipolar and recurrent depressive disorders. Thus, losses, physical illnesses, and deficient social support might have a formative influence in the origin of an isolated single episode of depression in the absence of a past or family history of mood disorders. This conceptualization was in part upheld in a previous paper by our group (Musetti et al. 1989) on late-onset depression that appeared triggered by stressors in the relative absence of familial-genetic factors.

The differentiation between “single” and “first” depressive episode could be obtained by the exclusion of those indicators of recurrence such as loaded pedigrees, bipolar family history, early onset, post-partum and psychotic episodes, and pharmacologic hypomania (Winokur 1974, Akiskal et al. 1979, 1983, Strober and Carlson 1982, Winokur et al. 1982), and pre-existing dysthymia (Keller et al. 1983, Klein et al. 1988).

In a previous study of 405 patients with MDE (Cassano et al. 1989), those with a single major depressive index episode in the absence of depressive, hypomanic, manic or mixed episodes were recognized as having distinct features characterized by a more frequent chronic course, a greater incidence of stressors preceding the episode, and an older age at onset than that of bipolar and recurrent depressions. However, as in the Pichot et al. study (1979), no clear-cut symptomatological differences emerged between younger and older depressives, even after controlling for the pathoplastic effect of aging. Neither our study, nor previous studies reviewed in Pichot and Pull (1981) have resolved the nosologic status of single-episode depressions, especially those with late-onset. For this reason, we decided to further investigate the characteristics of SE major depression among a larger population of 687 depressive patients, specifically aiming at the identification of a subgroup of depressives with a stable diagnosis of SE distinguishable from those with the potential for recurrence.
subsequent to index diagnosis. The attempt then was to characterize patients with SE on the basis of age at onset, affective temperaments, family history, stressors, chronicity, melancholic features, and psychotic symptoms. Subgroups of SE depressives were compared with recurrent unipolars to identify potential predictors of course and evolution. Therefore, the study attempts to shed light on the following main points:

1. the historical debate initiated by Kraepelin (1896) in the fifth edition of the Lehrbuch (only sixth edition exists in English 1990) on the existence of “involutional melancholia” or late-onset depression as a distinct entity;

2. clinical characterization of late-onset isolated SE as far as symptomatology, course and tendency to chronicity is concerned;

3. the role played by stressors, family history and temperamental dysregulation in the SE variety of depressive illness:

4. identifying SE in which subsequent recurrent unipolar to bipolar course is likely to occur.

Patients and Methods

The total study population comprised 687 major depressives – of whom 211 (30.7%) were male and 476 (69.3%) female – consecutively admitted to the University of Pisa Psychiatric Institute and affiliated clinical facilities. Their mean age at index evaluation was 50.26 years (SD 14.3) with a range of 18–82 years. To focus on as homogeneous as possible primary mood disorders, the following categories were excluded: patients whose depression was an understandable development in the setting of an organic mental disorder, mental retardation or a neurologic disorder: a psychoactive substance use disorder that dominated the clinical course: depressive concomitant with mental retardation, schizophrenia, panic, phobic, obsessive-compulsive and somatoform disorders, and anorexia-bulimia.

Diagnostic subtyping of subjects was accomplished with the Semistructured Interview for Depression (SID) (Cassano et al. 1987), which represents a collaborative effort between the Institute of Clinical Psychiatry of the University of Pisa, Italy, and the Section of Affective Disorder at the University of Tennessee, Memphis, USA (more recently transferred to the University of California at San Diego, USA). It is modified from the mood clinic semistructured interview (Akiskal et al. 1978), used extensively in University of Tennessee Clinical Research. The SID itself is designed to diagnose MDE (American Psychiatric Association 1987) and to collect systematic anamnestic data on number and duration of previous episodes, number of suicide attempts, temperamental aspects, interepisodic residual phenomena, response to previous treatment, “stressors” related to the onset of the index episode, and the presence of melancholia (or endogenous clinical features), as well as congruent and incongruent psychotic features. Family history data are collected by Winokur’s approach as incorporated into the family history method of the Research Diagnostic Criteria (Andreasen et al. 1977).

The major innovation in this instrument is the provision of operational criteria for depressive and hyperthymic temperaments representing the University of Tennessee modification (Akiskal and Mallyn 1987) of the Schneiderian descriptions (Schneider 1959). The depressive temperament requires the presence of at least five of the following items: 1. gloomy, pessimistic, humourless or incapable of fun; 2. quiet, passive or indecisive; 3. skeptical, hypercritical or complaining; 4. brooding and given to worry; 5. conscientious or self-disciplining; 6. self-critical, self-reproaching, or self-derogatory; 7. preoccupied with inadequacy, failure and negative events to the point of feeling morbid enjoyment at one’s own failures. As for the hyperthymic temperament, again at least five of the following items are required: 1. irritable, cheerful, over-optimistic or exuberant; 2. naive, overconfident, self-assured, boastful, bombastic or grandiose; 3. full of plans, improvized, carried away by restless impulses; 4. overtalkative; 5. warm, people-seeking or extroverted; 6. overinvolved and meddlesome; 7. uninhibited, stimulus-seeking or promiscuous. In our experience, reporting on clinical, age and gender correlates of smaller clinical subpopulations in this series (Cassano et al. 1989, Musetti et al. 1989, Perugi et al. 1990), both hyperthymic and depressive temperaments reflect easy-to-detect characteristics which are recognizable in index episodes and are not state-dependent, thereby supporting the utility of the present instrument in defining MDE subcategories on the basis of temperamental profiles. Klein’s (1990) experience with the depressive temperament also indicates lack of state dependency and longitudinal stability.

The SID permitted us to identify the following subtypes of primary MDE modified from the classificatory schema of Akiskal (1983a, b): 1. single-episode major depression; 2. recurrent unipolar major depression: 3. bipolar I (BD) disorder, MDE with a history of full-blown manic symptomatology: 4. bipolar II disorder (BDII), defined as MDE preceded or followed by hypomania; 5. MDE with pre-existing hyperthymic temperament (Akiskal and Akiskal 1988) – but in the absence of hypomania or mania – refers to apparently “unipolar” depressives with hyperthymic temperament (U-HT). In view of their small number, in previous publications (Cassano et al. 1988, 1989, Musetti et al. 1989, Perugi et al. 1990), we had tentatively combined groups 4 and 5 into the larger BII category. Given the much larger size of the present study population – and in accordance with current clinical convention in the present communication. MDE with hyperthymic temperament will be considered with unipolars, recurrent or single episode (U-HT).

The SID instrument partly derives from other operationalized procedures with published reliabilities (Andreasen et al. 1977, American Psychiatric Association 1987), as well as new procedures introduced by us to address the temperamental foundations of affective illness and the assignment of patients to the proposed bipolar and depressive subtypes. Intercentre (i.e. Pisa-Memphis) reliability has been documented elsewhere (Cassano et al. 1990) and we have now systemically used this instrument for over 5 years, conducting at least 1000 interviews, and psychiatrist participating in this series of studies have extensive and systematic training in the diagnostic approach, which has proved reliable. The semistructured face-to-face interview, which lasts 30–60 min, is well accepted by patients (Cassano et al. 1987). Information obtained from patients is routinely supplemented or corroborated by that obtained from significant others who accompany the patient to our clinic; this is of particular significance for familial psychopathology, and temperamental measures which are based on patients’ habitual functioning prior to affective episodes. All clinical information is gathered by psychiatrist with at least 7 years of post-doctoral clinical experience; all clinical data are ultimately presented of the present instrument in defining MDE subtypes on the basis of temperamental profiles. Klein’s (1990) experience with the depressive temperament also indicates lack of state dependency and longitudinal stability.

The SID approach to the diagnosis of manic and hypomanic episodes is documented in previous papers (Akiskal et al. 1989, Cassano et al. 1989). The specific criteria, derived from Akiskal et al. (1977), which distinguish mania from hypomania require one or more of the following: 1. meaningful conversation is difficult to maintain for any length of time; 2. euphoric or ecstatic mood deteriorates to querulous belligerence; 3. affective hallucinations or delusions of grandiose ability or identity, delusions of assistance or persecution, delusions of reference, and delusions of love; 4. loss of insight and judgment to such a degree that frenzied