CHAPTER I

INTRODUCTION

Depression is one of the many psychological problems that have plagued mankind throughout recorded history. The Biblical Patriarch Job suffered from severe depression, and feelings of guilt; in the first century, Plutarch graphically described behavior characteristics of the disorder; in 1921, Sir Robert-Burton devoted an entire treatise to “The Anatomy of Melancholy” and in the twentieth century depression became so widespread that it was called “The common cold of mental illness” (Miller & Seligman, 1973, p. 62). Like the common cold, depression is extremely widespread. But whereas the common cold rarely kills anyone, depression does.

Many famous people throughout history have suffered from depression. Winston Churchill wrote about the “black dog” that followed him throughout his life and finally immobilized him in his old age. Abraham Lincoln had bouts of depression and often dreamt of his own coffin. And artist Vincent van Gough cut off his own ear in a fit of despair (c.f. McNeil & Rubin, 1973, p. 488).

Epidemiological surveys demonstrate that depression is one of the more common mental disorders found in the general population (Sorenson, Rutter, & Aneshensel, 1991; Gupta, 1988). The prevalence of the disorder coupled with its association with suicide, has made depression the target of extensive research efforts into its causes, treatment and possible prevention. However, this research has been complicated by the lack of a clear definition of depression. Most experimental clinicians regard depression as a group of related behaviors, which have either an organic or psychological basis.

In an exhaustive study Grinker, Miller, Sabshin, Nunn, & Nunnaly (1961) found these “depressive behaviors” to include verbal statements of dysphoria, self-deprecation, guilt, material burden and fatigue; a low rate of motor behavior, and somatic complaints such as sleeplessness, loss of appetite and headaches.

According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-III-R; American Psychiatric Association, 1987) the two main categories of depressive disorders are major depression and dysthymia. To meet criteria for a major depressive episode, the individual must experience at least five of a list of nine symptoms during
the same 2-week period. At least one of the symptoms must be either depressed mood or loss of interest or pleasure. Furthermore, these symptoms must represent a change from previous functioning. In the case of children and adolescents, irritability may substitute for depressed mood. Among the remaining symptoms are change in weight or appetite, insomnia or hypersomnia, psychomotor agitation or retardation, fatigue or loss of energy, and psychological symptoms such as feeling of worthlessness or guilt, impaired ability to think or concentrate, recurrent thoughts of death, recurrent suicidal ideation, or a suicide attempt with or without a specific plan. Dysthymia for children and adolescents refers to chronic disturbance of mood involving either depressed or irritable mood for most of the day, more days than not, for at least one year, without the individual being symptom free for more than 2 months. Some of the symptoms of major depression should also be present. The DSM-III-R also includes a category of adjustment disorder with depressed mood when the predominant symptoms, such as depressed mood, fearfulness, and feelings of helplessness, occur in response to an identifiable psychological stressor.

Unfortunately, these behaviours can occur in a large number of combinations and to further complicate matters, they often occur in conjunction with other psychological problems such as generalized anxiety or hostility. Given the problems in definition, it is quite likely that the statement “The person is depressed” is one of the least informative communications in clinical practice (Derogatis, Klerman, & Lipman, 1972, p. 395). Indeed, it has been argued that the term depression might profitably be dropped from the clinician’s vocabulary. The term is practically undefinable anyway, and it infers to a hypothetical internal state that can be conceptualized only in terms of the behavior it is supposed to explain. Although one tends to agree with the crux of this argument, one also agree with Lazarus’s (1968) comment that “the temptation to deny depression as a subject matter for scientific enquiry must be resisted, if for no other reason than the fact that clinicians daily are consulted by thousands of people who say they feel depressed” (p. 84.).

WHAT IS COMORBIDITY?

The term “comorbidity” was first coined by Feinstein (1970) to refer to any distinct clinical entity occurring in a patient during the clinical course of the index disease under study. “Disease” and “Distinct” are two words that need to be underlined:
comorbidity was originally related to diseases in the medical sense; it was a word coined within the framework of the realistic interpretation of diseases in somatic medicine. Hence, comorbidity was referred to the co-occurrence of a real disease (a medical pathology clearly defined and with distinct boundaries) with a distinct clinical entity. A good example can be the comorbidity between a chronic heart disease and a femoral fracture in elderly patients. The causes of these two diseases may be unrelated (the thigh bone fracture being due to a fortuitous fall); nevertheless, the detection of this comorbidity is fundamental because the forced immobilization secondary to the bone fracture is likely to cause (via stagnation of blood flow and thrombosis) a significant worsening of the cardiocirculatory function. To sum up, within somatic medicine the comorbidity phenomenon is clinically useful, and it can be easily defined as “two or more diseases, with distinct aetiopathogenesis (or, if the etiology is unknown, with distinct pathophysiology of organ or system), that are present in the same individual in a defined period of time” (Vella, Aragona, & Alliani, 2000, p. 26). Although the previous definition can be easily used in somatic medicine, many problems arise when the concept of Comorbidity is transposed to psychiatry. Indeed, in psychiatry a realistic interpretation of mental disorders is suspect, the etiology of the most part of mental disorders being still largely unknown. As a consequence, “cases of true comorbidity are relatively rare since, for most disorders, we do not know enough about the underlying pathophysiology to be able to determine whether the disorders are truly clinically distinct” (First, 2005, p. 207).

COMORBIDITY AS A PSYCHIATRIC ANOMALY

While the term “comorbidity” refers to the presence of more than one mental disorder occurring in an individual at the same time, often the terms “comorbidity” and “dual diagnosis” are used interchangeably (Howard, Stubbs, & Arcuri, 2007). But the term “comorbidity” acknowledges that there may be more than two diagnoses for an individual, such as substance dependence/abuse and psychosis, anxiety or affective disorder. For these reasons the term “‘comorbidity’” is preferred. Hall, Lynskey, & Teeson (2001) warn against the narrow, too commonly accepted interpretation of comorbidity as the co-occurrence of schizophrenia and substance use disorders, and encourage a broader definition incorporating the other disorders such as anxiety and mood disorders (Teeson & Burns, 2001).
The inclusion of personality disorders arouses further concerns, diagnostically and for clinical practice, such as issues of self-harm, participation in crime, and the willingness of clinicians to engage with such presentations. Young people over the age of 18 years who have a depressive disorder or psychosis can also be diagnosed with a DSM-IV personality disorder (American Psychiatric Association, 2000). Those under 18 years of age may exhibit features of these disorders or be diagnosed with conduct disorder. Whatever the age, personality disorders, such as borderline personality disorder and antisocial personality disorder, raise particular concerns when clinicians attempt to provide interventions for young people who also meet criteria for substance dependence. The Australian National Survey of Mental Health and Wellbeing (1997; as cited by Teeson & Proudfoot, 2003) found that, within the general population, 18% of respondents met criteria for one DSM-IV diagnosis in the previous 12 months. Of this percentage, one in four also had at least one other mental disorder. Among adolescents in particular, in New South Wales (NSW), Australia, more than half of the young people in the National Survey of Mental Health and Wellbeing who had substance use disorders in the 12 months prior to being surveyed also had other mental health or physical problems (NSW Health, 2000a).

In the context of depression and anxiety, it can be stressed that depression and anxiety have long been categorized as separate clinical entities, but their coexistence is now considered to be as much the rule as the exception. According to some estimates, one-third to one-half of patients presenting with one disorder have some symptoms of the other. Moreover, recognition of the frequent comingling of anxiety and depressive systems has lead to the proposal of mixed anxiety-depression disorder as a discrete class of mental illness (American Psychiatric Association, 1994). According to a review of clinical reports (Katon & Roy-Byrne, 1991), 25% of depressed patients have a lifetime history of panic disorder, and 40% to 80% of patients with panic disorder have experienced a major depressive episode. Stein, Tancer, & Uhde (1990) studied the relationship between panic disorder and affective disorder in a population of 63 panic disorder patients. Approximately two-thirds of these patients had at least one lifetime episode of major depression; 63% of the comorbid group experienced a depressive episode before the onset of anxiety disorder, while 38% had an episode secondary to the onset of panic disorder. Few other studies have provided information about the order of onset, but published reports
suggest that panic disorder precedes depression in about one-third of patients, depression precedes panic disorder in one-third or more, and the two develop simultaneously in the remaining third (Lydiard, 1991).

High rates of comorbidity between depressive disorders and anxiety disorders have been documented in clinical and community samples of adults and children (Mineka, Watson, & Clark, 1998; Brady & Kendall, 1992). Investigators commonly reported that over half of patients with depressive disorders also have an anxiety disorder (Brown, Campbell, Lehman, Grisham, & Mancil, 2001; Mineka et al., 1998; Clark, 1989). This level of co-morbidity raises important questions about the boundaries between depressive and anxiety disorders (Watson, Kotov, & Gamez, 2006; Watson, 2005; Krueger, 1999), and has important implications for prognosis and treatment (Barlow, Allen, & Choate, 2004; Belzer & Schneier, 2004; Brown, Schulberg, Madonia, Shear, & Houck, 1996).

**THEORY-DRIVEN MODELS OF CO-MORBIDITY**

Major depressive disorder (MDD) and anxiety disorders (ANX) are common and highly co-morbid disorders (Kessler, Berglund, Demler et al., 2003; Angold, Costello, & Erkanli, 1999; Merikangas, Dierker, & Szamari, 1998; Mineka et al., 1998; Lewinsohn, Hops, Roberts, & Seeley, 1993; Maser & Cloninger, 1990). Research data have indicated a lifetime prevalence rate of 16.2% for Major depressive disorder (MDD) (Kessler et al., 2003) and 28.8% for anxiety disorder (ANX) (Kessler, Berglund, Demler et al., 2005). Fifty-nine percent of adults with lifetime major depressive disorder (MDD) also met criteria for lifetime anxiety disorder (ANX) (Kessler et al., 2003). Whereas major depressive disorder (MDD) onset is spread across adolescence and early adulthood (interquartile range from ages 18–43; Kessler et al., 2005), anxiety disorder (ANX) onset tends to be concentrated in a narrow developmental span characterized by an interquartile range from ages 6–20 (Kessler et al., 2005).

Two theoretical models of comorbidity between anxiety disorder (ANX) and major depressive disorder (MDD) that have received considerable research attention are direct causation and shared etiology. The direct causation model states that one disorder causes or lowers the threshold for the expression of the other disorder (Avenevoli, Stolar, Dierker, & Merikangas, 2001). To date, evidence indicates that
ANX often temporally precedes MDD (Merikangas, Zhang, Avenevoli et al., 2003; Breslau, Chilcoat, Schultz, & Peterson, 2000; Wittchen, 1998; Breslau, Schultz, & Peterson, 1995; Alloy, Kelly, Mineka, & Clements, 1990; Hagnell & Grasbeck, 1990; Regier, Burke, & Burke, 1990; Kovacs, Gatsonis, Paulauskas, & Richards, 1989) and predicts the course of MDD (Sanford et al., 1995), leading some to suggest that ANX may play a causal role in the development of MDD (Brady & Kendall, 1992). However, it is not yet clear whether the relationship is causal or explained by other factors.

The shared etiology model, also referred to as the correlated liabilities model (Neale & Kendler, 1995), posits that a common set of risk factors leads to the development of both MDD and ANX. Research has shown that MDD and ANX share several putative risk factors, such as severely stressful life events (D’Imperio, Dubow, & Ippolito, 2000; Cicchetti & Toth, 1998; Brown, 1993; Brown & Harris, 1993; Miller & Ingham, 1983; Finlay-Jones & Brown, 1981), socio-economic disadvantage, non-intact family structure, family dysfunction, and peer problems (Shanahan, Copeland, Costello, & Angold, 2008). Parental psychiatric disorders also have been implicated (Klein, Lewinsohn, Rohde, Seeley, & Shankman, 2003; Kovacs, Devlin, Pollock, Richards, & Mukerji, 1997; Harrington, Fudge, Rutter et al., 1993; Last, Hersen, Kazdin, Orvaschel, & Perrin, 1991; Puig-Antich, Goetz, Davies et al., 1989; & Turner, Beidel, & Costello, 1987). Thus, it is possible that common risk factors may account for a substantial proportion of the co-occurrence of MDD and ANX.

Olino, Klein, Lewinsohn, Rohde, & Seeley (2008) directly compared two models in a sample of 891 individuals from the Oregon Adolescent Depression Project who participated in up to four diagnostic assessments over approximately 15 years. Structural equation models were used to examine the relationship between depressive and anxiety disorders across different developmental periods (<14, 14-18, 19-23, 24-30 years of age). It was found that the three-factor model, positing that depressive and anxiety disorders were caused by a combination of shared and disorder-specific factors, provided a significantly better fit to the data than the one-factor model postulating that a single factor influences the development of both depressive and anxiety disorders. The authors extended the previous literature by directly comparing the one- and three-factor models of internalizing disorders in a large community sample of adolescents.
who received up to four semi-structured diagnostic assessments over approximately 15 years.

Comorbidity appears to aggravate the negative impact of depression and anxiety. It is associated with higher symptom severity in both disorders, more depression recurrences, increased academic difficulties, suicide attempts, physical illness, worse overall quality of life (Rush, Zimmerman, Wisniewski et al., 2005; Kessler, McGonagle, Swartz, Blazer, & Nelson, 1993; Lewinsohn, Rohde, & Seeley, 1995) and worse treatment outcomes (Young, Mufson, & Davies, 2006; Ledley, Huppert, Foa et al., 2005). The effects of comorbidity seem to go above and beyond its component disorders, and it is unclear why. Although comorbidity clearly exists, there is no consensus on its origins. Clarification of the mechanisms behind comorbidity is important on both theoretical and practical grounds, as it would guide understanding of psychopathology and inform treatment development.

Previous research has examined whether comorbidity is a result of a shared underlying substrate, such as negative affectivity (negative affectivity; Clark & Watson, 1991a), common genetic predispositions (Merikangas, 1990), or inadequate diagnostic criteria (Lilienfeld, Waldman, & Israel, 1994). However, little research has examined the possible role of psychosocial factors, which could potentially contribute to comorbidity in two ways. First, shared risk factors may lead to the development of both depression and anxiety. For example, Hankin, Abramson, Miller, & Haeffel (2004) showed that negative life events longitudinally predicted depression and anxiety, suggesting that both disorders may be traced to a common cause. Some evidence suggests, however, that different types of stressors predict depression and anxiety. For example, Finlay-Jones & Brown (1981) found that loss-related stressors predict depression, whereas danger-related events predict anxiety. Further exploration of the specificity of psychosocial risk factors to anxiety versus depression may guide the development of more detailed models.

Second, depression-anxiety comorbidity may result from an etiological relationship between the two disorders, in which symptoms of one disorder predispose toward the development of symptoms of the other. Several researchers have observed that anxiety tends to temporally precede depression (Essau, 2003; Wittchen, Kessler, Pfister, & Lieb, 2000; Orvaschel, Lewinsohn, & Seeley, 1995). In contrast, there are
few cases in which depression precedes first-onset anxiety, and pure depression (i.e., without a history of anxiety) is relatively rare (Dobson, Cheung, Maser, & Cloninger, 1990). Given its frequent temporal antecedence, some researchers (Wittchen, Beesdo, Bittner, & Goodwin, 2003; Stein, Fuetsch, Muller et al., 2001; Wittchen et al., 2000) have concluded that anxiety is likely to serve as a risk factor for the later development of depression. This does not exclude the possibility that depression also serves as a risk factor for anxiety, as there may be a reciprocal relationship between the two. In either case, one way in which one disorder could cause the development of the other is by causing the person to behave in ways that increase his or her exposure to etiological stressors. Once again, the identification of specific risk factors, concomitants, and consequences of depression and anxiety may allow for the development of a more informative model of comorbidity. Further development of both these models demands a clearer understanding of variables specifically associated with depression and anxiety. Although comorbidity appears to have a significant impact on disordered individuals, conceptual and practical implications of its presence have been largely ignored. In treatment outcome studies, comorbid conditions often serve to exclude individuals from entry. As such, we know that these individuals represent more severely impaired and disordered populations but we know little about how our treatments impact upon them. More importantly, perhaps, little is known about the pathways to comorbidity or, in other words, the conditions under which comorbidity occurs or why it occurs with such frequency. Surprisingly, little effort has been put forth to explicate the meaning behind the high comorbidity of anxiety and affective disorders in youth. As Rutter (1994) acknowledged: the observation of comorbidity or co-occurrence has to be regarded as a starting point from which to undertake research to investigate the mechanisms that might be involved. It does not in any way provide an explanation of the processes and, for this reason; it can only be regarded as a stimulus to further investigative work (p. 101). In this vein, four principal explanations for high rates of comorbidity can be deduced from the literature (Frances, Widiger, & Fyer, 1990). First, although two disorders such as anxiety and depression may be indicative of two distinct underlying constructs, the extent of overlapping definitional criteria may produce high rates of comorbidity. Second, it may be that comorbidity is caused by the splitting of a unitary latent construct into two (or more) categories. Third, two disorders can be comorbid because they share some underlying causal or risk factors. Last, one disorder may cause or put an individual at increased risk for a second disorder. Thus,
these first two explanations suggest that comorbidity of anxiety and depression is an artifact caused by the way in which the disorders are defined, whereas the last two explanations suggest that comorbidity is due to the nature of the disorders (e.g., etiology and associated outcomes).

CLINICAL SIGNIFICANCE

Anxiety disorders and depression, when experienced singly, are potentially and seriously debilitating disorders. The focus of psychiatric research is expanding to include patients with comorbid anxiety and depression. Growing evidence, for example, supports the clinical importance of the association between major depression and panic disorder, a common form of anxiety characterized by frequent and intense panic attacks. Several studies have called for greater specificity of the conceptualization of anxiety disorders (Merikangas et al., 2003; Widiger & Clark, 2000). Empirical work supports the division of anxiety disorders into fear and distress conditions, this overlap is particularly noted with regard to the distress condition of generalized anxiety disorder (GAD; Kessler, McGonagle, Zhao et al., 1994; Moffitt, Harrington, Caspi et al., 2007). Patients with comorbid panic and depressive disorders may have more severe symptoms and less favorable outcomes than patients with either disorder alone. Symptoms were worse and more frequent, for example, among patients in the comorbid group of the National Institute of Mental Health Epidemiologic Catchment Area (ECA) study, compared with patients in single-disorder groups (Andrade, Eaton, & Chilcoat, 1994). Patients with comorbid conditions more frequently experienced depressive symptoms that were associated with more severe depression, such as guilt, suicidal thoughts or attempts, and motor disturbances.

Another recent study (Grunhaus, Pande, Brown, & Greden, 1994) compared clinical symptoms and course of illness in 119 patients with major depression alone and 57 patients with major depression and concurrent panic disorder. Compared to patients in the depression-only group, patients in comorbid group:

1. Experienced more severe symptoms during the current episode of illness,
2. Had higher ratings on feelings of inadequacy, somatic anxiety, and phobia,
3. Reported symptoms and required treatment and hospital admission earlier, and
4. Required psychiatric hospitalization more frequently.
This finding of greater severity, disability, and chronicity of illness among those patients with comorbid panic disorder and depression has been demonstrated by a number of other groups as well (Grunhaus et al., 1994; Reich, Warshaw, Peterson et al., 1993; Van Valkenburg, Akiskal, Puzantian, & Rosenthal, 1984). Comorbid patients have been found to have an increased rate of suicidal ideation (Rudd, Dahm, & Rajab, 1993; Fawcett, 1992; Johnson, Weissman, & Klerman, 1990) and suicide attempts (Johnson et al., 1990), compared with patients with either disorder alone. An alarming 30% of individuals with mixed depression and panic disorders involved in the Zurich study had attempted suicide by age 28 (Vollarth & Angst, 1989). In a study of 954 patients with major depressive disorder who were followed longitudinally for 10 years, Fawcett (1992) found that the presence of panic attacks was one of the strongest predictors of completed suicide within the first year. Panic attacks were not, however, related to the likelihood of a completed suicide after the first year of follow up. It is clear that comorbid patients need to be regularly monitored for suicide risk.

Compared to non-co-morbid presentations of the disorders, co-morbid Major depressive disorder-Anxiety disorder (MDD–ANX) is associated with greater symptom severity (Bernstein, 1991; Coryell, Endicott, Andreasen et al., 1988; Mitchell, McCauley, Burke, & Moss, 1988), higher rates of suicidal behavior (Rohde, Clarke, Lewinsohn, Seeley, & Kaufman, 2001; Lewinsohn et al., 1995: Reich et al., 1993), higher rates of mental health treatment utilization but poorer treatment response (Brent, Kolko, Birmaher et al., 1998; Emslie, Weinberg, & Mayes, 1998; Lewinsohn et al., 1995), higher medical costs (Marciniak, Lage, Dunayevich et al., 2005), and an increased risk of recurrence (Emslie et al., 1998). Given the high level of overlap between MDD and ANX, and the severe impairment and cost incurred by their co-morbidity, understanding the development of co-morbid MDD–ANX represents a pressing need.

The rationale of the study in the context of clinical significance clearly reveals the seriously debilitating and damaging role of comorbidity of related disorders (e.g., depression and anxiety), though anxiety and depression, when experienced singly are also debilitating disorders. Mounting evidence suggests that patients who have coexisting anxiety disorder and depression can have an even worse prognosis than those with either condition alone. Comorbid patients may be more resistant to standard treatment, but many are successfully treated with cognitive or behavioural therapy and
antidepressants medication. Comorbidity may advance our knowledge. For example, if two disorders frequently coexist (e.g., depression and anxiety), this may shed some light on a possible common psychopathological pathway, therefore providing an important lead for innovative research and therapeutic approaches.

In the light of above assertion it can be acknowledged that the observation of comorbidity or co-occurrence has to be regarded as a starting point from which to undertake research to investigate the consequences that might be involved. It does not in any way provide an explanation of the processes and, for this reason, it can only be regarded as a stimulus to further investigative work. An attempt has been made in the current study to examine the consequences of comorbidity of anxiety and depression.

**OBJECTIVES**

The current study starts with the following objectives:

1. To compare the comorbid group, pure anxious group and pure depressive group on different measures of negative cognition, namely self-deprecation, hopelessness and dysfunctional attitudes.

2. To compare the comorbid group, pure anxious group and pure depressive group on suicide ideation.

3. To compare the comorbid group, pure anxious group and pure depressive group on extraversion.

4. To compare the comorbid group, pure anxious group and pure depressive on psychoticism.

5. To compare the comorbid group, pure anxious group and pure depressive group on different measures of perceived family environment, namely cohesion, expressiveness and conflict.