Insight into the heterogeneity of depressive disorders

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Chapter 5

The categorisation of Dysthymic Disorder: Can its constituents be meaningfully apportioned?

ABSTRACT

Background Since its introduction in DSM-III, the validity of Dysthymia has been debated. Our objective is to further examine the concept of Dysthymia in an outpatient sample, and explore whether its constituents can be meaningfully apportioned.

Methods 318 Patients attending the Black Dog Institute Depression Clinic were assessed by the Mini-International Neuropsychiatric Interview, and completed several self-report measures, in addition to clinical assessment by an Institute psychiatrist. The characteristics of patients with Major Depressive Disorder (MDD), Dysthymic Disorder and Double Depression were examined. Latent Class Analysis (LCA) and Latent Profile Analysis (LPA) were then conducted, with the aim of detecting distinct classes, based on depressive symptomatology and personality domains, respectively. Finally, clinicians' formulations of the study patients were examined.

Results Depression groups mainly differed on parameters of severity. Although LCA and LPA analyses indicated the presence of distinct classes, these only moderately correlated with the MINI-diagnosed groups. Finally, there was evidence for considerable heterogeneity within clinicians' formulations of Dysthymia.

Limitations Inadequate sample numbers limited the power of the LPA.

Conclusions Despite employing a variety of techniques, we were unable to obtain a clear homogeneous picture of Dysthymia. Rather, there was evidence for a distinct heterogeneity in clinician-derived diagnoses. These findings allude to the questionable discriminant validity of Dysthymia and may encourage future research and discussion on this important topic.

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INTRODUCTION

It is not uncommon for clinicians and researchers to describe patients as having 'Major Depression' and/or 'Dysthymic Disorder' - diagnoses introduced within the 1980 DSM-III manual (APA, 1980) and which have been largely viewed as describing depressive entities. Elsewhere (Parker and Manicavasagar, 2005) we have argued, however, for positioning Major Depression as a broad diagnostic domain subsuming multiple expressions of clinical depression. Conceptually, the same model might be applicable for Dysthymic Disorder – a depressive condition defined simply by fewer symptoms than Major Depression as well as by chronicity - with the individual having a depressed mood for most of the day for at least two years. At face value, it might be expected to include minor chronic as well as 'smouldering' depressive episodes, treatment resistant depressive conditions, and depression syndromes underpinned by perpetuating stressors or contributed to by multiple psychological and social factors. In this paper, we seek to critically examine the concept of Dysthymic Disorder and – in positioning it as a domain diagnosis rather than a diagnostic entity – seek to apportion constituent conditions.

The term Dysthymia can be traced historically to the Ancient Greek term to describe one who was "ill humoured" (Freeman, 1994) and therefore was primarily conceptualised as a personality style. Subsequently, it received categorisation as a clinical mood state by Flemming (1799–1880), albeit being positioned as a set of mood disorders rather than a single condition (Freeman, 1994). Although Kraepelin (1921) did not employ the term 'Dysthymia', he described the 'depressive temperament' as a substrate from which affective episodes subsequently developed (WPA Dysthymia Working Group, 1995). This distinction was subsequently recognised in the revised DSM (DSM-II; APA, 1968) which included a 'neurotic depression' - which emphasised personality aspects as opposed to symptoms – and which had the effect of classifying chronic depressive states as personality disorders and neuroses (WPA Dysthymia Working Group, 1995).

The term 'Dysthymia' then lay dormant until its reintroduction into psychiatry via DSM-III in 1980 – an introduction that was to trigger an intense conflict between the Task Force and psychodynamic practitioners. DSM-III's category of depressive disorders, including Dysthymic Disorder, weighted a biological model of depression – a weighting that was opposed by the psychodynamic practitioners. Concerned about the proposed loss of 'neurosis' and, of relevance here, of 'neurotic depression', they contended that the DSM Task Force was "focusing so much on the brain" and thereby "losing the mind" (Mayes and Horwitz, 2005). Shorter (2009) has argued that, to pacify such concerns, Dysthymia (with 'neurotic depression' in parenthesis) was introduced as part of a 'Neurotic Peace Treaty' – and with the "optics" being that, while Major Depression required pharmacotherapy, Dysthymia required psychoanalytic therapy. Of further symbolic relevance - and illustrating the victory of the biological-oriented movement over the psychoanalytic tradition - neurotic

depression was deleted in the subsequent revision of the DSM-IV (McPherson and Armstrong, 2006).

After its introduction in DSM-III, only minor changes in the definition of Dysthymic Disorder have been made, although controversy and challenges to its utility have long been evident. Epidemiological studies illustrating its lack of demarcation from other mood disorders across a broad range of demographic, clinical, psychosocial, family history and treatment response variables (McCullough et al., 2000, 2003; Klein et al., 2004) stimulated questions regarding its validity. In addition, the relatively low citation rate of 'Dysthymia' compared to Major Depression following its introduction led some to claim that "Major Depression was the only real depression left standing" (Shorter, 2009). Although Dysthymia citations did begin to rise in the early 1990s (McPherson and Armstrong, 2006), the relatively low rates indicate that diagnostic labels provided in manuals do not in themselves dictate the range of terms employed by professionals and individual clinicians.

In this paper, we examine the concept of Dysthymia, implementing both 'top down' and 'bottom up' procedures weighting key depressive symptoms (i.e. to determine if Dysthymia can be sub-typed by depressive features) and broad personality constructs respectively, and thus in line with the DSM-IV (APA, 1994; p. 732) contention that it is "controversial whether the distinction between depressive personality disorder and Dysthymic Disorder is useful". Using a top down approach we first examine whether Dysthymic Disorder can be demarcated from Major Depressive Disorder (and their composite state - so-called 'Double Depression'; Keller and Shapiro, 1982) using a formal case-finding measure and rating a variety of clinical and non-clinical variables or factors. The main objective of this approach is therefore to examine whether Dysthymia demonstrates discriminant validity. We then employ the data-driven techniques of Latent Class Analysis (LCA) and Latent Profile Analysis (LPA) to create clusters to determine constituent symptom and personality-based sub-classes or domains (i.e. a bottom up approach). Finally, in line with Robin and Guze's (1970) contention that clinical appraisal is a core validation strategy, we examine clinicians' formulations of these patients' conditions to determine if constituent heterogeneous sub-sets can be identified.

METHODS

Study population

Patients were recruited through the Depression Clinic at the Sydney-based Black Dog Institute. All patients gave consent and the study was approved by the University of New South Wales Ethics Committee. The Institute provides a state-wide service, offering diagnostic and management advice to patients referred by general practitioners or mental health professionals. Elements of the assessment process have been detailed elsewhere (see Parker et al., 2006a). Patients referred over the 2010-2011 period that reached criteria for

Major Depressive Disorder (MDD) or Dysthymic Disorder according to the Mini-International Neuropsychiatric Interview or MINI (Lecrubier et al., 1997) were included. Patients with a lifetime MINI diagnosis of Bipolar Disorder (I or II) or Schizoaffective Disorder were excluded. The total study population consisted of 318 patients. The MINI is a structured diagnostic instrument based on DSM-IV and ICD-10 criteria, with respectable reliability and validity (Sheehan et al., 1998). Three groups were then defined, namely: i) 'MDD only' (n=148) consisting of those meeting Major Depression but not Dysthymia criteria, ii) 'Dysthymia only' and otherwise termed as 'pure Dysthymia' (n=42) and iii) 'Double Depression' (n=128) for those with comorbid Dysthymia and MDD.

Principal assessment measures

Information on socio-demographic and clinical characteristics was derived from the Mood Assessment Program (MAP) and a self-report booklet. The MAP is an Institute-developed computerised assessment designed to assist clinicians with diagnostic decisions and the identification of contributing factors (Parker et al., 2008). The majority of patients complete both the MAP and the booklet prior to their clinical assessment. The final variables used to describe diagnostic groups were the patient's age, gender, depression severity (measured by the short version of the Quick Inventory of Depressive Symptoms – Self-Report measure or QIDS-SR; Rush et al., 2003), age of onset, family history, presence of a co-morbid anxiety disorder, bipolar symptoms (measured by the Mood Swings Questionnaire or MSQ; Parker et al., 2006b), severity of psychomotor disorder (measured by the CORE; Parker et al., 1995a, 1995b), level of functioning (assessed by a 6-item self-report measure assessing impairment across several key areas) and personality variables, as detailed in the next paragraph.

Variables selected for the LCA and LPA analyses

The variables selected for the LCA comprised the nine key depressive constructs outlined in the scoring guidelines for the QIDS-SR– namely; sleep disturbance, depressed mood, appetite or weight change, concentration problems, feelings of guilt, suicidal thoughts, anhedonia, fatigue and motor symptoms. The QIDS contains 16 items or symptoms which are usually rated on a 0 to 4 point scale and reflective of their presence over the preceding seven days (with coding roughly equating to 0=absent, 1=somewhat present, 2=moderately present, 3=largely present). In light of the small sample size and the number of items in the QIDS measure, items were dichotomized for the purposes of the LCA, where 0 represents the absence of a symptom and 1 the presence of a symptom.

The variables selected for the LPA correspond to the four domains of the NEO Personality Inventory (Costa and McCrae, 1995); namely, neuroticism, conscientiousness, introversion and agreeableness. These domains were derived from the MAP data – which includes the 81-item Temperament and Personality measure (T&P; Parker and Manicavasagar, 2005)

with patients indicating the relative descriptive relevance of each statement on a four-point rating scale (from 0="not true at all" to 3="very true") – and which allows quantification across those four constructs.

Clinical assessment

All patients underwent a detailed clinical assessment interview with a Black Dog Institute psychiatrist to generate a clinical diagnosis – with approximately one-third of patients also assessed by a second independent psychiatrist to derive a consensus diagnosis.

Statistical analyses

Principal top down analyses involved two-tailed chi-square tests for categorical variables and one-way analyses of variance (ANOVA) for continuous variables. Additional pairwise comparisons were performed to examine differences between groups. Total numbers differed in each analysis due to variations in the extent of missing data. Analyses conducted on the distribution of missing data indicated a random pattern across the MINI-diagnosed groups. All comparisons were conducted using SPSS Version 15 (SPSS , 2006).

Bottom up analyses (devoid of any *a priori* assumptions) involved the clustering of study patients according to a specified categorical (LCA) or continuous (LPA) outcome. LCA and LPA assume that one or more unobserved latent variables explain the associations among a set of observed symptoms. Both analyses commence with one class, with the assumption that one class optimally represents all patients. More classes are then added in order to determine the model providing the best fit. The LCAs and LPAs were conducted using M-plus version 5 (Muthén and Muthén, 2007). Unfortunately, subject numbers were too low to conduct a separate LCA and LPA on the pure Dysthymia patients (n=42).

There is currently no consensus regarding which criterion identifies the best number of classes so we used the following criteria: the Bayesian Information Criterion (BIC), sample size adjusted BIC (ssaBIC), the Lo-Mendell-Rubin likelihood ratio test (LMR), bootstrap likelihood ratio test (BLRT) and entropy. In determining the optimal number of classes, we gave preference to the LMR and ssaBIC (Tofighi and Enders, 2007) and BLRT (Nylund et al., 2007). To best identify clinically relevant classes, we only considered models with classes greater than five per cent.

RESULTS

Socio-demographic and clinical characteristics of the three MINI-diagnosed depressive groups (i.e. Major Depression, Dysthymia and their composite 'Double Depression') are provided in Table 1. Importantly, these groups did not differ by age, gender, age at depression onset, family history of depression, bipolarity scores. An increase in depression severity (as quantified by QIDS scores) and in levels of comorbid anxiety and functional impairment was evident across the Dysthymia, MDD and Double Depression groups, while the dysthymia group received the lowest ratings on psychomotor disturbance (as measured by the CORE), albeit not significant. In addition, patients in the Dysthymia group had significantly higher levels of agreeableness compared to the other two groups and there were significant differences on levels of neuroticism between the three groups.

Table 1. Characteristics of the study-population (n=318).

	Pure Major Depression	Pure Dysthymia	Double Depression	Overall statistics X^2/ F (df) p-value
	n=148 (46.5%)	n=42 (13.2%)	n=128 (40.3%)	
Demographics				
Age, mean (SD) (n=318)	39.4 (13.2)	41.1 (13.8)	41.0 (13.2)	ns
Gender (% female) (n=318)	54.7	50.0	52.3	ns
Clinical characteristics*				
Depression severity (QIDS-SR -score), mean (±SD) (n=318)	15.6 (4.4) [a,b]	11.9 (4.8) [a,c]	17.5 (4.0) [b,c]	26.8 (2) <.001
Age of onset of depression, mean (±SD) (n=193)	19.8 (10.5)	18.9 (8.2)	19.8 (13.1)	ns
Family history of depression (yes %) (n=190)	73.6	88.5	75.3	ns
Comorbid anxiety disorder (%) (n=193)	32.4[b]	28.6[c]	45.3[b,c]	6.4 (2) .04
Bipolarity score, mean (±SD) (n=193)	16.0 (23.4)	13.4 (21.8)	13.9 (21.3)	ns
Total CORE score, mean (±SD) (n=315)	3.1 (4.6)	2.0 (3.2)[c]	3.8 (5.1)[c]	ns
Overall functioning (count- higher is lower level), mean (±SD) (n=193)	15.1 (4.6)[a]	12.4 (6.1)[a,c]	16.3 (4.8)[c]	6.8 (2) <.001
Personality and temperament scale (n=193)				
Neuroticism, mean (±SD)	12.8 (4.4)[b]	13.7 (4.4)	14.2 (4.3)[b]	ns
Conscientiousness, mean (±SD)	16.8 (6.2)	16.9 (5.2)	16.4 (6.7)	ns
Introversion, mean (±SD)	11.6 (5.2)[b]	12.6 (4.3)	13.5 (5.2)[b]	ns
Agreeableness, mean (±SD)	3.4 (2.8)[a]	5.0 (3.4)[a,c]	3.7 (2.6)[c]	3.2 (2) .04

*Due to missing data on specific parameters, total numbers differ per analysis. [a,b,c] Significant difference (p<.05) between: a=MDD versus Dysthymic Disorder, b=MDD versus Double Depression, c= Dysthymic Disorder versus Double Depression

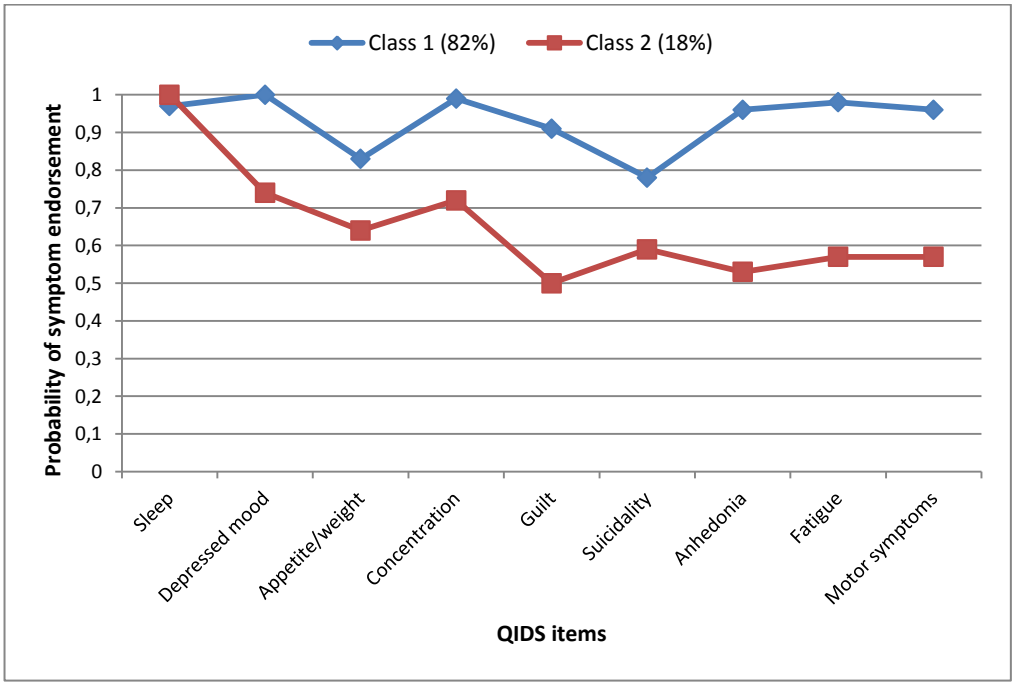
Table 2. Parameters of fit of Latent Class and Latent Profile Analyses.

Classes	Maximum Likelihood	BIC	ssa BIC	Lo-Mendell-Rubin		BLRT	Entropy	Proportion of individuals in class					
				2LL	p			1	2	3	4	5	6
Latent Class Analysis, based on QIDS (n=318)													
2	**-894.4**	**1898.3**	**1838.0**	**130.8**	**0.02**	**<.001**	**0.78**	**0.82**	**0.18**				
3	-880.8	1928.6	1836.7	26.8	0.06	<.001	0.71	0.64	0.33	0.03			
4	-872.3	1969.2	1845.5	17.0	0.23	0.7	0.76	0.65	0.13	0.20	0.03		
Latent Profile Analysis, based on personality domains (n=193)													
2	-2221.0	4510.4	4469.2	60.0	0.001	<.001	0.63	0.53	0.47				
3	-2204.7	4504.11	4447.1	32.6	0.04	<.001	0.69	0.47	0.43	0.10			
4	-2196.0	4513.0	4440.2	17.4	0.5	0.04	0.70	0.10	0.37	0.19	0.34		
5	**-2187.2**	**4521.8**	**4433.1**	**17.5**	**0.5**	**0.04**	**0.72**	**0.37**	**0.13**	**0.07**	**0.09**	**0.35**	
6	-2179.4	4532.5	4428.0	15.7	0.4	0.07	0.80	0.11	0.03	0.36	0.26	0.16	0.09

Abbreviations: BIC= Bayesian Information Criterion; 2LL= 2 log likelihood; ssaBIC= Sample Size Adjusted BIC

We then performed the bottom up, data-driven procedures to examine whether LCA and LPA could identify clinically meaningful depressive subtypes. In Table 2, we first report the parameters of fit of the LCA model. While the BIC and LMR tests favoured a 2-class model, the ssaBIC and BLRT tests were supportive of a 3-class model. Since the third class comprised a small minority of patients (less than 5%) - and so questioned its clinical relevance - the 2-class model was selected for interpretation. Figure 1 plots the probability of endorsement per construct for the two identified latent classes. The first class (prevalence=82.1%) was characterised by a high endorsement of all depressive constructs. The second class (prevalence=17.9%) was similarly characterised by a high endorsement of all depressive constructs, albeit of lesser magnitude than class 1. In essence, as opposed to any significant qualitative difference in the nature of symptoms between the two classes, most of the differences were due to symptom severity – that is, a quantitative difference.

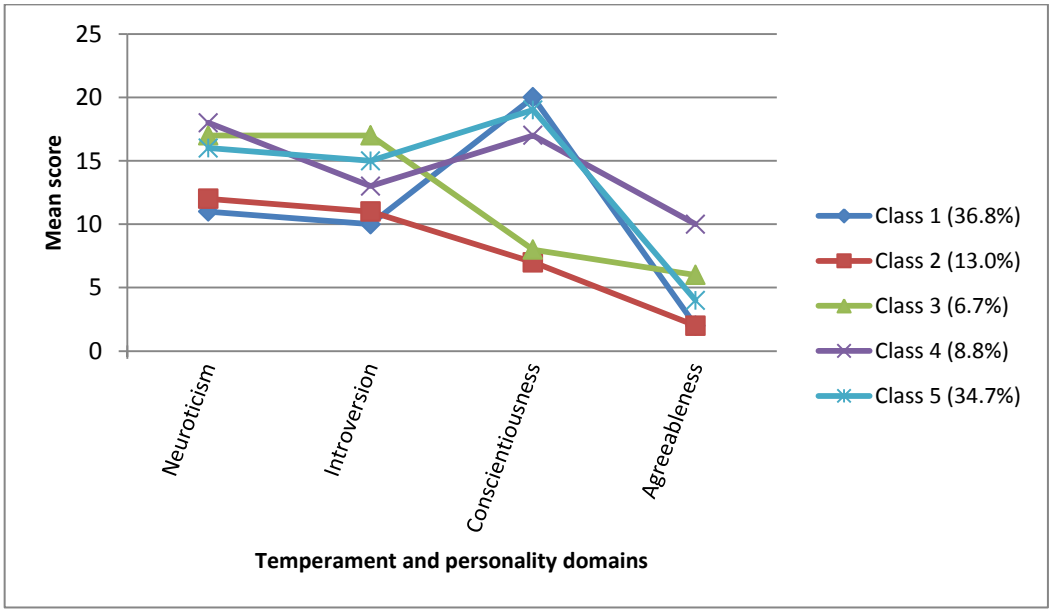
Figure 1. Probability of symptom endorsement per class in LCA, based on depressive symptomatology, assessed by the QIDS-SR (n=318).



LPA data analyses were conducted on the quantified personality domains, and with results provided in Table 2. Analyses were conducted on 193 study patients since some patients did not complete the MAP. Two parameters (BIC and LMR-test) favoured a 3-class model, one (BLRT) favoured a 5-class model, while both the ssaBIC and entropy tests favoured models involving more classes. However, small class prevalences were evident from the 6-class model onwards – a finding probably reflecting the creation of spurious classes (Hipp and Bauer, 2006). The optimal performance of the ssaBIC (Tofighi and Enders, 2007) and BLRT

(Nylund et al., 2007) has been previously demonstrated. We therefore decided that the 5-class model provided the best fit to the observed data. The estimated means for each domain are displayed in Figure 2. The main findings were that classes with high levels of neuroticism and introversion (class 3=6.7%; class 4=8.8% and class 5=34.7%) were distinguishable from classes with low levels (class 1=36.8%, class 2=13.0%), and that classes could be further distinguished by levels of conscientiousness - with classes 2 and 3 characterised by low conscientiousness levels. While there were no significant differences on levels of agreeableness across most classes, class 4 exhibited higher levels on that scale compared to the other classes.

Figure 2. Estimated means per class in LPA, based on personality domains, assessed by the T&P-measure (n=193).



The distributions of LCA-derived and LPA-derived classes were then compared across the three study groups, with results provided in Table 3. Participants in the pure Dysthymia group were distinctly more likely to be allocated to class 2 of the LCA solution (characterised by less severe depression), while the majority of those with major depression (MDD alone, or Double Depression) were allocated to class 1 (characterised by more severe depression). In the LPA-solution, the majority of patients (36.8%) across all MINI-diagnosed groups were allocated to class 1. Class 5 was characterised by a preponderance of patients with Major Depression (MDD alone, or Double Depression), whereas class 4 was characterised by a considerable proportion of 'pure Dysthymics' thus suggesting the presence of a 'pure Dysthymic' profile (Table 3). As previously demonstrated (Ormel et al., 2004), MDD is associated with higher levels of neuroticism in depressed– compared to euthymic– states. Therefore, depression severity might inflate associations between neuroticism (and other

personality domains) and depression measures. To examine this further, we conducted post-hoc analyses using multivariate, multinomial logistic regression analyses to test the association between MINI-diagnosed groups and class membership, with and without adjustment for depression severity. In unadjusted analyses, Dysthymia was associated with class 4 membership (OR 6.8 [95% CI 1.50-29.6]); however, this association no longer reached significance after adjustment for depression severity (OR 4.4 [95% CI 0.86-22.3]) (class 5 is reference in both). There were no other significant associations between MINI-diagnosed groups and LPA-classes.

Finally, in line with Robin and Guze's (1970) contention that clinical appraisal is a core validation strategy, we examined clinicians' formulations of these patients' conditions to determine if constituent heterogeneous sub-sets could be identified. Six principal diagnoses were identified; namely, Non-Melancholic Depression, Melancholic Depression, Dysthymic Disorder, Bipolar Disorder, Anxiety Disorder and an 'other' disorder. Table 4 presents the distribution of clinicians' diagnoses across the Dysthymic and Double Depression groups. In the pure Dysthymic group, there were a high proportion of patients with non-melancholic depression, in contrast to the Double Depression group where melancholic depression was more frequently diagnosed. Notably, no study patients were diagnosed with a Dysthymic Disorder and - despite the fact that a MINI diagnosis of Bipolar Disorder served as an initial study exclusion criterion - a considerable number of participants with pure Dysthymia (25.0%) and Double Depression (21.8%) were diagnosed as having a Bipolar Disorder. Finally, we examined the characteristics of those patients in the pure Dysthymia group, with groupings made according to the clinicians' diagnosis. As can be seen in Table 5, while patients in this group were diagnosed with a variety of conditions, the limited sample size prevented firm conclusions regarding the statistical significance of any group differences on demographics, clinical characteristics, or personality and temperament factors.

Table 3. Comparison of prevalence rates of DSM-categories across LCA and LPA derived classes, and comparison of prevalence rates of LCA-derived classes across LPA-derived classes.

	Pure Major Depression	Pure Dysthymia	Double Depression	Overall statistics X^2/ F (df) p-value
LCA classes (n=318)				
	n=148 (46.5%)	n=42 (13.2%)	n=128 (40.3%)	
Class 1 (severe) (82.1%)	89.7[a]	48.8[a, c]	90.6[c]	46.8 (2)
Class 2 (moderate) (17.9%)	10.3[a]	51.2[a, c]	9.4[c]	<.001
LPA classes (n=193)				
	n=78 (40.4%)	n=29 (15.0%)	n=86 (44.6%)	
Class 1 (36.8%)	41.0	44.8	30.2	
Class 2 (13.0%)	15.4	3.4	14.0	
Class 3 (6.7%)	5.1	3.4	9.3	ns
Class 4 (8.8%)	9.0[a]	20.7[a,c]	4.7[c]	
Class 5 (34.7%)	29.5	15.0[c]	44.6[c]	

LCA classes	Class 1 Severe n=164 (85.2%)	Class 2 Moderate n=29 (14.8%)		
LPA classes				
Class 1 (36.8%)	34.8	50.0		
Class 2 (13.0%)	13.7	7.1		
Class 3 (6.7%)	7.5	3.6		ns
Class 4 (8.8%)	7.5	10.7		
Class 5 (34.7%)	36.6	28.6		

[a,b,c] Significant difference (p<.05) between: a=MDD versus Dysthymic Disorder, b=MDD versus Double Depression, c= Dysthymic Disorder versus Double Depression

Table 4. Clinical diagnoses across pure Dysthymia and Double Depression (MINI-diagnoses) (n=164).

	Pure Dysthymia	Double Depression	Overall	Overall statistics X^2/ F (df) p-value
	n=42 (24.7%)	n=128 (75.3%)	n=170 (100%)	
Clinician's diagnoses (n=164)				
Non-melancholic depression	19 (47.5%)	31 (25.0%)	50 (30.5%)	
Melancholic depression	7 (17.5%)	41 (33.1%)	48 (29.3%)	
Dysthymic disorder	0	0	0	10.6 (4) .03
Bipolar disorder I/II	10 (25.0%)	27 (21.8%)	37 (22.6%)	
Anxiety disorder	4 (10.0%)	17 (13.7%)	21 (12.8%)	
Other	0	8 (6.5%)	8 (4.9%)	

Table 5. Characteristics of participants within pure Dysthymic Disorder (n=42).

	Non-Melancholic	Melancholic	Bipolar	Anxiety	Overall p-value
	n=20 (47.6%)	n=7 (16.7%)	n=11 (26.2%)	n=4 (9.5%)	
Demographics					
Age, mean (SD) (n=42)	41.7 (12.7)	44.7 (13.4)	35.0 (14.1)	45.0 (15.3)	ns
Gender (% female) (n=42)	57.9	14.3	70.0	50.0	ns
Clinical characteristics					
Depression severity (QIDS-SR score), mean (±SD) (n=42)	11.3 (4.0)	10.4 (5.0)	12.8 (5.3)	10.3 (4.6)	ns
Age of onset of depression, mean (±SD) (n=27)	18.1 (8.0)	26.8 (11.4)	14.0 (3.7)	21.0 (7.3)	ns
Family history of depression (yes %) (n=24)	81.8	100.0	100.0	100.0	ns
Comorbid anxiety disorder (%) (n=42)	31.6	14.3	40.0	50.0	ns
Total CORE score, mean (±SD) (n=42)	1.5 (2.7)	2.6 (3.3)	2.9 (4.5)	1.3 (1.9)	ns
Overall functioning (count-higher is lower level), mean (±SD) (n=27)	11.1 (5.3)	13.5 (8.3)	12.3 (5.2)	12.0 (9.2)	ns
Personality and temperament scale (n=27)					
Neuroticism, mean (±SD)	13.8 (2.7)	11.7 (3.5)	16.4 (3.8)	11.6 (8.2)	ns
Conscientiousness, mean (±SD)	17.4 (5.4)	14.3 (7.8)	18.0 (4.5)	16.3 (3.2)	ns
Introversion, mean (±SD)	12.9 (3.8)	14.6 (3.6)	11.4 (6.4)	16.6 (1.8)	ns
Agreeableness, mean (±SD)	3.7 (2.5)	4.3 (5.3)	6.6 (3.3)	5.0 (4.4)	ns

DISCUSSION

The main objective of this study was to empirically examine the concept of Dysthymia as currently defined by DSM-IV, and to determine if constituent conditions could be identified. To address this objective, we implemented both top down and bottom up procedures. These procedures suggested that Dysthymia has questionable discriminant validity with the majority of differences between MINI-diagnosed groups (i.e. MDD, Dysthymic Disorder and Double Depression) evident only on parameters of severity, thus suggestive of quantitative - rather than qualitative - differences. While LCA and LPA analyses identified classes based on depressive symptomatology and personality domains, comparison of these classes with the three study groups showed only marginal overlap. In addition, there was only a moderate association between the classes identified by LCA and LPA, indicating heterogeneity within the depressive subtypes and difficulties in meaningfully apportioning any constituent states. Finally, clinicians' diagnoses were examined for the pure Dysthymia and Double Depression groups, and while there was evidence of a relatively clear-cut clinical distinction, sample numbers were insufficient to identify any condition-specific correlates.

While there are several similarities between current and previous study results - particularly the lack of profound differences between MDD, Dysthymia and Double Depression groups on a variety of parameters (McCullough et al., 2000, 2003; Klein et al., 2004) - there are some notable inconsistencies with previous literature. The small proportion of comorbid anxiety disorders among the Dysthymia group is in contrast to that of previous studies. For example, Klein et al. (2004) found a higher proportion of comorbid anxiety conditions in participants with Dysthymia when compared to those with episodic MDD or chronic MDD. Second, in accordance with other researchers (e.g. Rapaport et al., 2005; Goldney and Fisher, 2004), the present study found that participants with Dysthymia were less impaired than those with MDD - while others have demonstrated the opposite (Buist-Bouwman et al., 2004) or equivalent levels of functioning (Rhebergen et al., 2010; Subodh et al., 2008).

Turning to personality constellates, LPA analyses identified distinct classes based on personality domains. In a recently conducted meta-analysis, Kotov et al. (2010) demonstrated that Dysthymia was more strongly associated with extraversion and conscientiousness than MDD - although there was no clear association between agreeableness and depressive disorders. However, when post-hoc analyses were conducted in the present study to examine the association between MINI-diagnosed groups and personality profiles, class membership was no longer associated with MINI-diagnosed groups after depression severity was adjusted. These findings suggest that although distinct personality profiles might be present within the broad category of Dysthymia, MINI diagnoses do not meaningfully capture its constituents.

The limited concordance between the various groups (i.e. MINI-diagnosed groups, LCA and LPA classes) is indicative of considerable heterogeneity that cannot be captured by one model. Data-driven techniques (LCA and LPA) defined models that greatly differed in number of classes (2 versus 5), thus suggesting a variable number of subtypes, and comparison of LCA and LPA classes with DSM categories indicated that these classes only moderately overlapped. For example, approximately half of the patients in the Dysthymic group were allocated to the severe class in the LCA, despite the fact that Dysthymia is – by definition – a mild depressive disorder. Similarly, half of the Dysthymic patients were allocated to the first class in the LPA - a percentage similar to those with MDD - although it has previously been argued that Dysthymic disorder is more 'trait-like' than MDD (Klein et al., 2011). Other studies that have used data-driven techniques have found evidence of an inadequate fit between DSM-categories and classes. For example, Rhebergen et al. (2011) conducted Latent Class Growth Analyses (LCGA) and found that over 50% of persons with a diagnosis of Dysthymia and Double Depression (by definition representing a chronic course) were best defined by classes characterized by a lack of chronicity.

Results regarding clinician diagnoses indicated considerable diversity within the MINI-diagnosed Dysthymia group. Similar results have been reported by Serretti et al. (1999), who also found the variance explained by the clusters to be relatively low and more indicative of a broad heterogeneity in disease presentation. In the current study, two findings are especially noteworthy. First, a considerable proportion of patients in the Dysthymic and Double Depression groups were diagnosed as having a Bipolar Disorder, despite the fact that a MINI diagnosis of Bipolar Disorder initially served as a study exclusion criterion. Previous researchers have highlighted the link between Dysthymia and Bipolar spectrum disorder (Akiskal, 2001; Brunello et al., 1999; Niculescu and Akiskal, 2001), with key findings that Dysthymic disorder in childhood is associated with an increased risk of developing Major Depression and Bipolar Disorder (Kovacs et al., 1994) and, secondly, a higher rate of Bipolar Disorder in relatives of Dysthymic persons when compared to those with a unipolar Major Depression (Klein et al., 1988; Cassano and Savino, 1993), although this latter finding was not supported in a later study by Klein et al. (2004).

Of further note, none of the patients in the Dysthymic group actually received a clinical diagnosis of a Dysthymic Disorder- at least by our clinicians-, suggesting its low clinical utility. Patients with Dysthymia are likely to have other comorbid conditions (e.g. anxiety, personality disorders and/or MDD) with high levels of functional impairment so that clinicians may focus on judged primary conditions rather than the more chronic 'low-grade' depressive state (Klein and Santiago, 2003). Since the Institute is a tertiary referral clinic, its sample of patients is weighted to those with a more severe depressive condition and so clinicians may be inclined to focus on the more severe aspects of psychopathology.

To our knowledge, this study is the first to examine the concept of Dysthymia by implementing both top down and bottom up approaches within the same study population. In addition, we explored the clinical diagnoses of all study patients, in line with previous recommendations that clinical appraisal should play a central role in validation strategies (Robins and Guze, 1970). In addition, an extensive array of self-report questionnaires was completed by patients, enabling the examination of differences on a variety of factors between the three depressive groups. However, sample numbers were reduced somewhat due to incomplete data on several measures, thus limiting the power of the LPA. Furthermore, and as previously noted, our clinic is a tertiary referral clinic and therefore weighted to patients with a more severe depressive condition. It is possible that in other samples comprising patients with milder symptomatology, differences between MDD and Dysthymia may be more profound - with the emergence of distinct personality profiles. Finally, only patients with a lifetime MINI diagnosis of Bipolar Disorder or Schizoaffective Disorder were excluded. Hence, the heterogeneity of dysthymia may have become more pronounced by our inclusion of those with a comorbid anxiety or personality disorder.

To conclude, despite employing a variety of techniques to examine Dysthymic Disorder, we did not obtain a clear homogeneous picture (other than variation by severity) and instead encountered distinct heterogeneity.. Findings of this nature allude to the questionable discriminant validity of a frequently used psychiatric disorder - and provide further fuel to the debate currently being considered for DSM-V that the term ‘Dysthymia’ and ‘Chronic Major Depression’ be abandoned and subsumed into an enveloping ‘Chronic Depressive Disorder’. However, that approach would risk the creation of another heterogeneous domain diagnosis characterised by certain factors such as depression duration or persistence rather than weight aetiological or treatment differentiation. As truly valid conditions (in psychiatry and medicine) can always be dimensionalised along severity, duration and persistence parameters, a dimension-based diagnostic model can always be implemented. However, if it overrides identification of intrinsically differing conditions or aetiological priorities that might argue for quite differing interventions, its clinical relevance is compromised. Such concerns are intrinsic to the concept of Dysthymia and would benefit from debate.

REFERENCES

American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders (second edition) (DSM-II). 1968. American Psychiatric Association, Washington, DC.

American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders (3rd revised edition) (DSM-III). 1980. American Psychiatric Association, Washington, DC.

American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders (4th edition) (DSM-IV). 1994. American Psychiatric Association, Washington, DC.

Akiskal HS. Dysthymia and cyclothymia in psychiatric practice a century after Kraepelin. Journal of Affective Disorders 2001; 62: 17-31.

Brunello N, Akiskal H, Boyer P, Gessa GL, Howland RH, Langer SZ, Mendlewicz J, Paes de Souza M, Placidi GF, Racagni G, Wessely S. Dysthymia: clinical picture, extent of overlap with chronic fatigue syndrome, neuropharmacological considerations, and new therapeutic vistas. Journal of Affective Disorders 1999; 52: 275-290.

Buist-Bouwman MA, Ormel J, de Graaf R, Vollebergh WA. Functioning after a major depressive episode: complete or incomplete recovery? Journal of Affective Disorders 2004; 82: 363-371.

Cassano GB, Savino M. Chronic major depressive episode and dysthymia: comparison of demographic and clinical characteristics. European Psychiatry 1993; 8: 277-279.

Costa PT, McCrae RR. Domains and facets: hierarchical personality assessment using the revised NEO personality inventory. Journal of Personality Assessment 1995; 64: 21-50.

Freeman HL. Historical and nosological aspects of dysthymia. Acta Psychiatrica Scandinavica 1994; suppl. 383: 7-11.

Goldney RD, Fisher LJ. Double depression in an Australian population. Social Psychiatry and Psychiatric Epidemiology 2004; 36: 921-926.

Hipp JR, Bauer DJ. Local solutions in the estimation of growth mixture models. Psychological Methods 2006; 11: 36-53.

Keller MB, Shapiro RW. "Double depression": superimposition of acute depressive episodes on chronic depressive disorders. American Journal of Psychiatry 1982; 139: 438-442.

Klein DN, Taylor ET, Dickstein S, Harding K. Primary early onset dysthymia: comparison with primary non bipolar non chronic major depression on demographic, clinical, familial, personality and socioenvironmental characteristics and short term outcome. Journal of Abnormal Psychology 1988; 97: 387-398.

Klein DN, Santiago NJ. Dysthymia and chronic depression: Introduction, classification, risk factors, and course. Journal of Clinical Psychology 2003; 59: 807-816.

Klein DN, Shankman SA, Lewinsohn PM, Rohde P, Seeley JR. Family study of chronic depression in a community sample of young adults. American Journal of Psychiatry 2004; 161: 646-653.

Klein DN, Kotov R, Bufferd SJ. Personality and Depression: Explanatory models and review of the evidence. Annual Review of Clinical Psychology 2011; 7: 269-295.

Kotov R, Gamez W, Schmidt F, Watson D. Linking "big" personality traits to anxiety, depressive, and substance use disorders: a meta-analysis. Psychological Bulletin 2010; 136: 768-821.

Kovacs M, Akiskal HS, Gatsonis C, Parrone PL. Childhood-onset dysthymic disorder: Clinical features and prospective naturalistic outcome. Archives of General Psychiatry 1994; 51: 365-374.

Lecrubier Y, Sheehan D, Weiller E, Amorim P, Bonora I, Sheehan K, Janavs J, Dunbar G. The MINI International Neuropsychiatric Interview (M.I.N.I.) A Short Diagnostic Structured Interview: Reliability and Validity According to the CIDI. European Psychiatry 1997; 12: 224-231.

Mayes R, Horwitz AV. DSM-III and the revolution in the classification of mental illness. Journal of the History of the Behavioral Sciences 2005; 41: 249-267.

McCullough JP, Klein DN, Keller MB, Holzer CE, Davis SM, Kornstein SG, Howland RH, Thase ME, Harrison WM. Comparison of DSM-III-R chronic major depression and major depression superimposed on dysthymia (double depression): validity of the distinction. Journal of Abnormal Psychology 2000; 109: 419-427.

McCullough JP, Klein DN, Borian FE, Howland RH, Riso LP, Keller MB, Banks PLC. Group comparisons of DSM-IV subtypes of chronic depression: Validity of the distinctions Part II. Journal of Abnormal Psychology 2003; 112: 614-622.

McPherson S, Armstrong D. Social determinants of diagnostic labels in depression. Social Science and Medicine 2006; 62: 50-58.

Muthén LK, Muthén BO. Mplus User's Guide. Fifth Edition. 2007. Muthén and Muthén, Los Angelas, CA.

Niculescu AB, Akiskal HS. Proposed endophenotypes of dysthymia: evolutionary, clinical and pharmacogenomic considerations. Molecular Psychiatry 2001; 6: 363-366.

Nylund KL, Asparouhov A, Muthén BO. Deciding on the number of classes in latent class analysis and growth mizture modeling: A Monte Carlo simulation study. Structural Equation Modeling 2007; 14: 535-569.

Ormel J, Rosmalen J, Farmer A. Neuroticism: a non-informative marker of vulnerability to psychopathology. Social Psychiatry and Psychiatric Epidemiology 2004; 39: 906-912.

Parker G, Hadzi-Pavlovic D, Brodaty H, Austin MP, Mitchell P, Wilhelm K, Hickie I. Sub-typing depression, II. Clinical distinction of psychotic depression and non-psychotic melancholia. Psychological Medicine 1995a; 25: 825-832.

Parker G, Hadzi-Pavlovic D, Hickie I, Brodathy H, Boyce P, Mitchell P, Wilhelm K. Sub-typing depression, III. Development of a clinical algorithm for melancholia and comparison with other diagnostic measures. Psychological Medicine 1995b; 25: 833-840.

Parker G, Manicavasagar V. Modelling and managing the depressive disorders- a clinical guide. 2005. Cambridge: Cambridge University Press.

Parker G, Fletcher K, Barrett M, Manicavasagar V. The Black Dog Institute Depression Clinic: a subtyping model in practice. Australasian Psychiatry 2006a; 14: 300-303.

Parker G, Hadzi-Pavlovic D, Tully L. Distinguishing bipolar and unipolar disorders: an isomer model. Journal of Affective Disorders 2006b; 96: 67-73.

Parker GB, Fletcher K, Hyett MP. The Mood Assessment Program: a computerised diagnostic tool for deriving management plans for mood disorders. Medical Journal of Australia 2008; 188: S126-128.

Rapaport MH, Clary C, Fayyad R, Endicott J. Quality-of-life impairment in depressive and anxiety disorders. American Journal of Psychiatry 2005; 162: 1171-1178.

Rhebergen D, Beekman AT, de Graaf R, Nolen WA, Spijker J, Hoogendijk WJ, Penninx BWJH. Trajectories of recovery of social and physical functioning in major depression, dysthymic disorder and double depression: a 3-year follow-up. Journal of Affective Disorders 2010; 124: 148-156.

Rhebergen D, Lamers F, Spijker J, de Graaf R, Beekman AT, Penninx BWJH. Course trajectories of unipolar depressive disorders identified by latent class growth analysis. Psychological Medicine 2011; 7: 1-14.

Robins E, Guze SB. Establishment of Diagnostic Validity in Psychiatric Illness: Its Application to Schizophrenia. American Journal of Psychiatry 1970; 126: 107-111.

Rush AJ, Trivedi MH, Ibrahim HM, Carmody TJ, Amow B, Klein DN, Markovitz JC, Ninan PT, Kornstein S, Manber R, Thase ME, Kocsis JH, Keller MB. The 16-Item Quick Inventory of Depressive Symptomatology (QIDS), clinician rating (QIDS-C), and self-report (QIDS-SR): a psychometric evaluation in patients with chronic major depression. Biological Psychiatry 2003; 54: 573-583.

Serretti A, Jori MC, Casadei G, Ravizza L, Smeraldi E, Akiskal H. Delineating psychopathologic clusters within dysthymia: a study of 512 out-patients without major depression. Journal of Affective Disorders 1999; 56: 17-25.

Sheehan DV, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E, Hergueta T, Baker R, Dunbar GC. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. Journal of Clinical Psychiatry 1998; 59: Suppl 20: 22-33.

Shorter E. Before Prozac: the troubled history of mood disorders in psychiatry. 2009. Oxford: Oxford University Press.

SPSS. SPSS for Windows: version 15.0. 2006. SPSS: Chicago.

Subodh BN, Avasthi A, Chakrabarti S. Psychosocial impact of dysthymia: A study among married patients. Journal of Affective Disorders 2008; 109: 199-204.

Tofighi D, Enders CK. Identifying the correct number of classes in a growth mixture models. In: Hancock GR and Samuelson KM (Eds.), Advances in latent variable mixture models. 2007. Information Age. Greenwich, CT, pp 317-341.

WPA Dysthymia Working Group. Dysthymia in Clinical Practice. British Journal of Psychiatry 1995; 166: 174-183.