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Research report

The utility of a classificatory decision tree approach to assist clinical differentiation of melancholic and non-melancholic depression

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ABSTRACT

Background: Studies suggest that differentiating melancholic from non-melancholic depressive disorders is advanced by use of illness course as well as symptom variables but, in practice, potentially differentiating variables are generally positioned as having equal value. Judging that differentiating features are more likely to vary in their signal intensity, we sought to determine the number of features required to effect differentiation and their hierarchical order.

Methods: The 24-item clinician-rated Sydney Melancholia Prototype Index (SMPI-CR) was completed for 364 unipolar depressed patients. The sample was divided into two cohorts according to the recruitment period. An RPART classification tree analysis identified the most discriminating SMPI items in the development sample of 197 patients, and examined the sensitivity and specificity of the diagnostic decisions, then sought to replicate findings in a validation sample of 169 patients.

Results: Independent analyses of putative SMPI items identified only seven items as required to discriminate those with clinically-diagnosed melancholic or non-melancholic depression when the conditions were examined separately. An RPART analysis considering differentiation of melancholic and non-melancholic depression in the total samples retained five of those items in the classification tree, three of which were non-symptom items, and with 92% sensitivity and 80% specificity in the development sample. This reduced item set showed 93% sensitivity and 82% specificity in the validation sample.

Limitations: Our clinical judgment of melancholic or non-melancholic depression may not correspond with the clinical logic employed by other clinicians.

Conclusion: Only five SMPI items were required to derive a succinct and efficient decision tree, comprising high sensitivity and specificity in differentiating melancholic and non-melancholic depression. Current study findings provide an empirical model that could enrich clinicians' approach to differentiating melancholic and non-melancholic depression.

1. Introduction

Melancholia (and synonymous diagnostic terms such as endogenous, endogenomorphic, Type A and 'typical' depression) has been alternately positioned as a categorical depressive disease and as a more 'severe' manifestation of clinical depression. Irrespective of the validity of those respective binarian and unitarian models, ascriptions for melancholia have been maintained with some consistency over recent decades (Jackson, 1986; Parker et al., 1996; Taylor and Fink, 2006; Parker et al., 2007) and include a distinctive pattern of symptoms and signs, primary genetic and biological origins (Stenstedt, 1962; Maes et al., 1991), a low placebo response (Brown, 2007), and a superior response to physical treatments such as antidepressant medications and electroconvulsive therapy than to the psychotherapies (Bolwig and Madsen, 2007; Parker et al., 2013). Its suggested differential treatment response (in comparison to the residual non-melancholic depressive conditions) argues strongly for its clinical identification.

Melancholia has, however, largely resisted pristine definition by clinical features alone, and with attempts predictably limited by the lack of any validating 'gold standard' laboratory test and often by analytic approaches which derive dimensions rather than generate categories. Most studies have, however, continued to analyse symptom sets alone, leading to an emphasis on so-called 'endogeneity symptoms' capturing mood nuances (e.g. anhedonia), 'vegetative' items (e.g. loss of appetite), diurnal variation and psychomotor disturbance in providing discrimination. However, an overview of evaluative studies (Parker et al., 1996) indicated that many such endogeneity symptoms show minimal or no separation across melancholic and non-melancholic depressive conditions. DSM (since DSM-III and continuing with DSM-5) has a symptom set of criteria for its melancholia specifier,

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comprising one mandatory symptom (i.e. anhedonia or mood non-reactivity) and also requiring three of six other criteria symptoms. However, as five of the listed melancholia symptom criteria are also criteria for major depression, there is limited separation of those meeting major depression criteria with – as against those without – melancholia. Such a lack of 'cleavage' then compromises studies seeking to identify differing causes and preferential treatment modalities across those with 'true' melancholic and non-melancholic depressive episodes. Criteria-based manuals (such as the DSM and ICD systems) accord equal weightings to any identified symptom and thus do not allow that melancholia's constituent symptoms may vary considerably in their classificatory impact. Finally, symptoms showing equal weightings may do so simply as a consequence of being synonyms. Thus, symptom-based measures risk having intrinsic and practical limitations, and argue for considering the impact of a wider set of clinical features. For example, psychiatrists have previously suggested that 'contextual' criteria be added to the DSM-IV diagnostic approach, which is largely restricted to symptom checklists (Wakefield and Schmitz, 2014; Maj, 2014).

Respecting the historical weighting given to psychomotor disturbance (see Jackson, 1986) – with Berrios (1988) observing that, in classical antiquity, melancholia was more "defined in terms of… reduced behavioural output" rather than as a mood state – and that psychomotor symptoms are included in many measures of melancholia, such as the Bech–Rafaelsen Melancholia Scale (Bech and Rafaelsen, 1980) and the Hamilton Endogenomorphy Subscale (Thase et al., 1983), there have also been attempts to differentiate melancholia by the presence of signs of psychomotor disturbance. Representative measures include the Depression Retardation Rating Scale (Widlőcher, 1983) and the CORE measure (Parker and Hadzi-Pavloic, 1996), but we progressively judged the latter as limited in requiring ratings to be undertaken when the depressed person is at or near the nadir of their episode and when young people with classical symptoms of melancholia may not show signs of psychomotor disturbance as overtly as older people.

We can conclude that melancholia has no identified symptom or sign (or aggregated set of clinical features) that provides absolute or even highly distinctive differentiation from non-melancholic depressive states, and with only some clinical features showing over-representation at best. This could reflect melancholia not being a categorical entity or – and the model we favour – that it is a disease entity but that its constituent symptoms and signs vary across individuals and thus argue more for prototypic (or 'fuzzy set') definition. Such a model is not unique in medicine. For example, individuals with Parkinson's disease may show quite varying clinical features, with its diagnostic accuracy advanced by clinicians adopting a prototypic approach to symptom appraisal and considering illness correlates as well as evaluating symptoms.

We suggest that identifying and differentiating melancholic depression from non-melancholic depressive conditions should be approached in a similar way – identifying a prototypic pattern of clinical features and illness correlates and moving beyond considering symptom features only to include illness course variables and then seeking to weight their contributory impact on diagnostic differentiation. One such previous strategy is informative. The Newcastle Scales (Carney et al., 1965) had, in addition to symptoms, a range of non-symptom variables (e.g. personality, anxiety, developmental factors, treatment response), with features accorded differing weightings, with scores on the melancholia scale being strongly predictive of response to electroconvulsive therapy.

We therefore developed the SERDEX (Self-Report of Depressive Experiences) measure (Parker et al., 2012) for differentiating melancholic and non-melancholic depression. Items (see Appendix A) include depressive symptoms, general levels of emotional dysregulation and interpersonal functioning, as well as distal and proximal stressors. Raters are invited to tick all 'characteristic' items from either the left-hand column A or the right-hand column B (with sets of 12 putative melancholic and 12 putative non-melancholic items in each column respectively). Raters are also requested to judge whether the individual's prototypic pattern is best captured by column A, column B, is somewhat closer to A than to B, is somewhat closer to B than to A, or is an equal mix or A and B descriptors. Analyses of data generated by 141 clinically depressed participants showed that context or causal variables (e.g. episodes coming 'out of the blue' or being 'disproportionately severe') appeared to differentiate melancholic from non-melancholic patients more strongly than melancholic depressive symptoms. Analyses of self-reported forms favoured a scoring strategy of subtracting the sum of B items from the sum of A items and with a cut-off on that 'difference score' of ≥ 2 having a sensitivity of 75% and specificity of 70% in assigning patients who had received a 'clinical' diagnosis of melancholia.

We then examined the measure's psychometric properties using an equivalent clinician-rated version and in separate samples of patients with unipolar depression (Parker et al., 2013a) and bipolar depression (Parker et al., 2013b). In both studies, the clinician-rated measure showed superior discrimination in identifying melancholia compared to the patient-rated version. An ROC analysis quantified that, in the unipolar depressed patients, a 'difference' score of 4 or more A ('melancholic') than B ('non-melancholic') descriptors had a sensitivity of 0.84, specificity of 0.92, positive predictive value of 0.90 and negative predictive value of 0.88. In the bipolar depressed sample, an ROC analysis also identified a cut-off score of 4 or more for melancholia as providing optimal discrimination, and with a sensitivity of 0.83, specificity of 0.92, positive predictive value of 0.88 and negative predictive value of 0.88. Hence, the clinician-rated version of the SERDEX measure (now named the Sydney Melancholia Prototype Index or SMPI) is preferred to the self-report version, and with the replicated cut-off score (across unipolar and bipolar patients) advancing confidence in the strategy and in the actual measure.

While checklists generally assign equal weights to criteria symptoms (a component of the polythetic model), clinicians are more likely to apply a 'pattern analysis' approach, according diagnostic signals differing weightings in judging whether the patient's illness corresponds to a prototypic pattern or not. The key risk to such an approach is of the clinician adopting – and then reifying – an intuitive and idiosyncratic approach which may have no validity. Thus, we report the development of an empirical decision tree approach involving analysis of SMPI data (in a larger sample than studied previously with the measure) to develop a hierarchical model that assumes a gradient in the signal differentiation of candidate features and specifies its nuances and level of discriminating accuracy at each step of the hierarchy. It so respects clinical decision making but seeks to provide an empirically developed application for the clinical differentiation of melancholic and non-melancholic depression.

2. Methods

The sample was recruited from the Depression Clinic at the Black Dog Institute in Sydney, a tertiary referral service providing diagnostic and management advice. The Human Research Ethics Committee for the University of New South Wales approved the study protocol. All participants were over the age of 18 years. A study description was provided and a written informed consent was obtained.

2.1. Materials

The clinician-rated SMPI (see Appendix A) required the six Clinic psychiatrists to select all salient (symptom and non-symptom) item features identified in their clinical interview, whether