

Distinguishing bipolar disorder and borderline personality disorder: an exploration of clinical and neuroscience informed approaches.

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Abstract

Bipolar disorder and borderline personality disorder are common psychiatric diagnoses. One is a mood disorder with a strong genetic basis while the other is a disorder of personality commonly related to abusive experiences in childhood. Despite contrasting aetiologies they can be difficult to differentiate because of overlapping clinical presentations and symptoms. Diagnostic accuracy is important because of their polarised treatment approaches: long term treatment with mood stabilizers for bipolar disorder and psychotherapy for borderline personality disorder.

A qualitative study of psychiatrists revealed comprehensive knowledge of the diagnostic criteria however, many expressed the view that diagnostic criteria did not assist diagnostic differentiation. These findings were validated in a large electronic survey of UK psychiatrists. A detailed study of actual diagnostic processes revealed that this scepticism appeared to influence actual practice. Clinicians largely ignored diagnostic criteria but continued to give diagnoses.

Age and IQ matched women with bipolar disorder, borderline personality disorder and a healthy control group were compared in a series of cognitive tasks. Borderline personality disorder was associated with a failure to establish and maintain reciprocal cooperation in a game theoretic measure of social exchange. This behavioural change was not seen in euthymic bipolar disorder. Borderline personality disorder was also associated with an insensitivity to reward and losses in a risky decision-making task. Using a simple two-choice reaction task post error slowing was significantly amplified in the borderline group despite overall reaction times and error rates being similar in all three groups.

Clinical diagnostic practice as revealed in this study is not adequate to reliably differentiate between bipolar disorder and borderline personality disorder. Laboratory measures of social exchange, decision making and post-error slowing highlight fundamental difficulties in borderline personality disorder not seen in euthymic bipolar disorder. These findings support the differentiation of bipolar disorder from borderline personality disorder and offer translational models for developing and evaluating new treatments for borderline personality disorder.

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This thesis contains approximately 38,000 words

1. INTRODUCTION

Bipolar disorder and borderline personality disorder are common psychiatric diagnoses. Bipolar disorder is a mood disorder characterised by periods of elated (mania) and low mood (depression) (see figure 1.1). The disorder is subcategorised on the basis of the severity of manic episodes into bipolar-1, bipolar-2 and bipolar not otherwise specified (NOS) (appendix 1). Bipolar disorder is categorised in the Diagnostic and Statistical Manual-IV (DSM-IV) (American Psychiatric Association, 1994) as an axis-1 mood disorder. By contrast borderline personality disorder is an axis-2 disorder which is characterised by a pervasive pattern of difficulties which include mood instability and recurrent suicidal gestures (see figure 1.2). I have chosen to use DSM-IV classifications of borderline personality disorder and bipolar disorder as DSM-5 was published after data collection had commenced and at the time of writing the updated Structured Clinical Interview for DSM Disorders (SCID) has yet to be published. The changes in the diagnostic criteria from DSM-IV to DSM-5 are discussed later in this chapter.

The boundary between borderline personality disorder and bipolar disorder is a source of clinical uncertainty. Both borderline personality disorder and broadly defined bipolar disorder are common psychiatric diagnoses in the adult population with similar prevalences of 4-6% (Angst, 1998, Grant et al., 2008). The two are commonly comorbid with around 30% of euthymic bipolar disorder patients found to fulfill criteria for borderline personality disorder on screening using standardised interviews (Kay et al., 1999, Brieger et al., 2003, Carpenter

et al., 1995). Comorbidity as high as 50.1% of those with bipolar-1 was reported in wave 2 of the National Epidemiologic Survey of Alcohol and Related Conditions (NESARC) (Grant et al., 2008). This indicates an association well beyond chance. However, the similarities and the differences between the disorders and their co-occurrence are increasingly a source of considerable confusion (Benazzi, 2000a, Paris, 2004, 2007, Smith et al., 2004, Ruggero et al., 2010, Yatham et al., 2009), not least because treatment recommendations for each disorder are currently so polarized. Bipolar disorder is often emphasized to be a disorder requiring long term treatment with mood stabilizers (Goodwin and Consensus Group of the British Association for Psychopharmacology, 2009); borderline personality disorder to be a disorder best treated by psychotherapy (National Collaborating Centre for Mental Health, 2009).

Criteria for a Manic Episode

A. A distinct period of abnormally and persistently elevated, expansive, or irritable mood, lasting at least 1 week (or any duration if hospitalization is necessary):

B. During the period of mood disturbance, three (or more) of the following symptoms have persisted (four if the mood is only irritable) and have been present to a significant degree:

1. inflated self-esteem or grandiosity
2. decreased need for sleep (e.g., feels rested after only 3 hours of sleep)
3. more talkative than usual or pressure to keep talking
4. flight of ideas or subjective experience that thoughts are racing
5. distractibility (i.e., attention too easily drawn to unimportant or irrelevant external stimuli)
6. increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation
7. excessive involvement in pleasurable activities that have a high potential for painful consequences (e.g., engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments)

C. The symptoms do not meet criteria for a Mixed Episode.

D. The mood disturbance is sufficiently severe to cause marked impairment in occupational functioning or in usual social activities or relationships with others, or to necessitate hospitalization to prevent harm to self or others, or there are psychotic features.

E. The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication, or other treatments) or a general medical condition (e.g., hyperthyroidism).

Note: Manic-like episodes that are clearly caused by somatic antidepressant treatment (e.g., medication, electroconvulsive therapy, light therapy) should not count toward a diagnosis of Bipolar I Disorder.

Criteria for a Mixed Episode

A. The criteria are met both for a Manic Episode and for a Major Depressive Episode (except for duration) nearly every day during at least a 1-week period:

B. The mood disturbance is sufficiently severe to cause marked impairment in occupational functioning or in usual social activities or relationships with others, or to necessitate hospitalization to prevent harm to self or others, or there are psychotic features.

C. The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication, or other treatment) or a general medical condition (e.g., hyperthyroidism).

Criteria for a Hypomanic Episode

A. A distinct period of persistently elevated, expansive, or irritable mood, lasting throughout at least 4 days, that is clearly different from the usual non depressed mood:

B. During the period of mood disturbance, three (or more) of the following symptoms have persisted (four if the mood is only irritable) and have been present to a significant degree:

1. inflated self-esteem or grandiosity
2. decreased need for sleep (e.g., feels rested after only 3 hours of sleep)
3. more talkative than usual or pressure to keep talking
4. flight of ideas or subjective experience that thoughts are racing
5. distractibility (i.e., attention too easily drawn to unimportant or irrelevant external stimuli)
6. increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation
7. excessive involvement in pleasurable activities that have a high potential for painful consequences (e.g., engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments)

C. The episode is associated with an unequivocal change in functioning that is uncharacteristic of the person when not symptomatic.

D. The disturbance in mood and the change in functioning are observable by others.

E. The episode is not severe enough to cause marked impairment in social or occupational functioning, or to necessitate hospitalization, and there are no psychotic features.

F. The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication, or other treatment) or a general medical condition (e.g., hyperthyroidism).

Note: Hypomanic-like episodes that are clearly caused by somatic antidepressant treatment (e.g., medication, electroconvulsive therapy, light therapy) should not count toward a diagnosis of Bipolar II Disorder

Figure 1.1. The diagnostic criteria for bipolar affective disorder (American Psychiatric Association, 1994).

Criteria for borderline personality disorder

A pervasive pattern of instability of interpersonal relationships, self-image, and affects, and marked impulsivity beginning by early adulthood and present in a variety of contexts, as indicated by five (or more) of the following:

1. frantic efforts to avoid real or imagined abandonment. **Note:** Do not include suicidal or self-mutilating behaviour covered in Criterion 5.
2. a pattern of unstable and intense interpersonal relationships characterized by alternating between extremes of idealization and devaluation
3. identity disturbance: markedly and persistently unstable self-image or sense of self
4. impulsivity in at least two areas that are potentially self-damaging (e.g., spending, sex, substance abuse, reckless driving, binge eating). **Note:** Do not include suicidal or self-mutilating behaviour covered in Criterion 5.
5. recurrent suicidal behaviour, gestures, or threats, or self-mutilating behaviour
6. affective instability due to a marked reactivity of mood (e.g., intense episodic dysphoria, irritability, or anxiety usually lasting a few hours and only rarely more than a few days)
7. chronic feelings of emptiness
8. inappropriate, intense anger or difficulty controlling anger (e.g., frequent displays of temper, constant anger, recurrent physical fights)
9. transient, stress-related paranoid ideation or severe dissociative symptoms

Figure 1.2. The diagnostic criteria for borderline personality disorder (American Psychiatric Association, 1994)

Aims of this thesis.

The aims of this thesis are:

1. To explore the the views and experiences of NHS clinicians in differentiating between borderline personality disorder and bipolar disorder. I will use a qualitative approach as little is known about clinicians' views. Qualitative research is a form of inquiry that analyses information through language and behaviour in natural settings (Lincoln and Guba, 1985) . It captures information about values and perceptions that is not well conveyed in quantitative data. I will use the themes

generated in the qualitative interviews to develop a questionnaire which will be used to validate the initial findings in a larger group of psychiatrists.

2. To explore the practice of clinicians when they are assessing patients in whom borderline personality disorder and bipolar disorder are likely differential diagnoses. I will audiorecord diagnostic assessments and systematically analyse coverage of the diagnostic criteria in order to identify the clinical features clinicians use to make diagnostic decisions. Diagnostic information will be combined with all available clinical information to assess whether clinical practice is concordant with the views expressed in the qualitative study.
3. To test the hypothesis that borderline personality disorder and bipolar disorder will exhibit important divergent behaviours in the context of social interaction and decision making in a laboratory setting. Age- and IQ-matched participants with borderline personality disorder or bipolar disorder, and a healthy control group will be invited to complete a series of computerised tasks.

Are borderline personality disorder and bipolar disorder really expressions of the same disorder?

Diagnosis starts with symptoms and complaints described by the patient themselves or by others. The phenomenology that clinicians generate on the basis of clinical interviews is usually the starting point for differential diagnosis. Both borderline personality disorder and bipolar disorder are characterised by chronic affective instability and impulsivity, which led to suggestions that they

belong to the same spectrum of illness (Deltito et al., 2001, Akiskal et al., 1985, 2004, Paris et al., 2007, Smith et al., 2004). Early commentators argued that since affective instability was the core symptom of borderline personality disorder (from which other difficulties emerged), borderline personality disorder would be more appropriately diagnosed and managed within the wider spectrum of bipolar disorders (Akiskal et al., 1985). Bipolar disorder had emerged from Angst's epidemiological studies (Angst, 1980, 1998) as a continuum defined by different severities of mood elevation from mania (bipolar disorder-I), through conservatively defined hypomania (bipolar disorder-II), to states of mood elevation that could be shorter and or milder bursts of over-activity (bipolar disorder NOS or not otherwise specified) (see appendix 1). The bipolar disorder-NOS group was ill-defined in DSM-IV, and the diagnosis was rarely made 20 years ago. Indeed, the relative vagueness of the borderline personality disorder and especially bipolar disorder-NOS constructs meant that they were probably often confused. It was argued somewhat optimistically that reframing borderline personality disorder to be part of the bipolar spectrum would be of broad benefit to clinicians and patients alike (Smith et al., 2004). Thus, pharmacological treatment options might be extrapolated from bipolar disorder, and a move away from the personality diagnosis could reduce stigma.

The actual criteria for diagnosis of borderline personality disorder are shown in figure 1.2. Five of the nine features of borderline personality disorder are required for the diagnosis and, as it happens, five features clearly overlap with bipolar disorder, or rather, bipolar disorder patients may exhibit these features (see table 1.1). Usually they would occur in acute episodes of hypomania or

depression, but obviously, hypomania and depression may be relatively chronic and a tick-box approach to phenomenology could confuse the anger or irritability of borderline personality disorder with the episodic expression of irritability which is allowed as a clinical equivalent of (hypo)mania in bipolar disorder. So, mis-diagnosis should not be surprising. Nevertheless, to confuse the two requires a misreading of transient symptoms in bipolar disorder as characterological. The key clinical feature of borderline personality disorder is its pervasive pattern of instability of interpersonal relationships, self-image, and affects, and marked impulsivity that begins by early adulthood and is present in a variety of contexts. Sustained mood elevation or mania is not a feature of borderline personality disorder whereas repeated anger, hostility, self-harm reactive to interpersonal stress and extreme rejection sensitivity are axiomatic. However, there is an increasing body of evidence to suggest that euthymia is dominated by subsyndromal symptoms such as mood instability and heightened impulsivity (Holmes et al., 2011, Perroud et al., 2011).

Five or more of the following for borderline personality disorder:	Present in (hypo)mania	Present in depression	Present in euthymia
frantic efforts to avoid real or imagined abandonment	NO	NO	NO
a pattern of unstable and intense interpersonal relationships - extremes of idealization and devaluation	NO	NO	NO
identity disturbance: markedly and persistently unstable self-image or sense of self	NO	NO	NO
<i>Impulsivity, self-damaging (e.g., spending, sex, substance abuse, reckless driving, binge eating).</i>	YES	NO	(YES)
<i>recurrent suicidal behavior, gestures, or threats, or self-mutilating behavior</i>	NO	YES	NO
<i>affective instability due to a marked reactivity of mood (e.g., intense episodic dysphoria, irritability, or anxiety usually lasting a few hours and only rarely more than a few days)</i>	NO	NO	YES
chronic feelings of emptiness	NO	NO	NO
<i>inappropriate, intense anger or difficulty controlling anger</i>	YES	NO	NO
<i>transient, stress-related paranoid ideation or severe dissociative symptoms</i>	YES	NO	NO

Table 1.1 the overlap between the diagnostic criteria for borderline personality disorder and bipolar disorder in the three different phases of bipolar disorder.

Impulsivity

Impulsivity is a clinically imprecise term conveying the sense of 'acting before thinking: premature, poorly considered action, dissociated from sound decision making'. Impulsivity is said to be common in both disorders, and both groups score highly on the Barratt Impulsiveness Scale (BIS). Impulsivity appears to persist during euthymia in bipolar disorder (Swann et al., 2004, Perroud et al.,

2011), although one study has reported significantly higher self-reported impulsivity in women with borderline personality disorder when compared to those with bipolar-2 disorder (Henry et al., 2001). In both groups impulsivity has been shown to be negatively correlated with age (Swann et al., 2004, Zanarini et al., 2007). Impulsivity is linked with recurrent suicidal acts (one of the diagnostic criteria for borderline personality disorder) in borderline personality disorder; however, such gestures are not uncommon in bipolar disorder, with approximately 1/3 of patients making one or more attempts (Bellivier et al., 2011). Recent work suggests that impulsivity is not a reliable marker for suicidal behaviour in bipolar disorder however as no difference in impulsive traits has been observed between bipolar disorder with and without a history of attempted suicide (Perroud et al., 2011) .

Recurrent suicidal behaviour

Suicidal behaviour is a significant cause of morbidity and mortality in bipolar disorder (Anderson et al., 2012, Hawton et al., 2005) with an estimated annual risk of attempted suicide of 0.9% per year and a lifetime risk of up to 50%. (Gonda et al., 2012, Chen and Dilsaver, 1996, Simon et al., 2007). Suicide accounts for 15-19% of all deaths in bipolar patients at long term follow up (Abreu et al., 2009). Between 60 and 70% of borderline patients will attempt suicide (Gunderson, 2008) with the rate of suicide reported to be between 8 and 10% (Black et al., 2004, American Psychiatric Association, 2001). While there are no studies that directly compare suicide rates in the two diagnostic groups

the current literature appears to suggest that rates are higher in those with bipolar disorder.

The frequent recurrence of self-harm may be a more helpful differentiator as a recent systematic review found that 41% of those with borderline personality disorder engaged in such acts on more than 50 occasions (Oumaya et al., 2008). In adolescent bipolar populations however, 1/3 report having engaged in self harm with nearly 2/3 of those who engage in self-harm having done so on more than one occasion (Esposito-Smythers et al., 2010). While recurrence may be a useful factor in distinguishing the two diagnoses retrospectively its utility is likely to be limited at initial assessment.

Affective instability

Affective instability is a widely used term which incorporates frequent affective shifts, disturbances in affect intensity, excessive reactivity to emotional cues and overdramatic expression (Koenigsberg et al., 2002). It is common in the general population with 13.9% of those interviewed in the Adult Psychiatric Morbidity Survey 2007 (Marwaha et al., 2013) positively endorsing the SCID-II item “do you have lots of sudden mood changes?”. People with borderline personality disorder have much greater affective instability than healthy controls (Ebner-Priemer et al. (2007a), 2007b) and it is also a common feature of bipolar disorder (Paris, 2004, Smith et al., 2004).

Self report and clinician-administered measures have been found to be useful in distinguishing these specific characteristics of affective instability in borderline personality disorder from bipolar disorder (Reich et al., 2011), although the extent to which these measures might be useful in differentiating the two diagnoses is unknown. Affective instability in bipolar disorder is classically described as alternating between elation and depression, whereas in borderline personality disorder elation is not a feature (Henry et al., 2001, Koenigsberg et al., 2002). In a small inpatient sample, bipolar disorder was found to be associated with greater intensity shifts between euthymia–elation and depression–elation on the Affective Lability Interview for Borderline Personality Disorder (ALI-borderline personality disorder), whereas borderline personality disorder was associated with significantly more intense shifts between euthymia–anxiety, euthymia–anger, anxiety–depression, and depression–anxiety (Reich et al., 2011). In addition the role of psychosocial stressors in precipitating affective shifts in borderline personality disorder tends to be prominent (Henry et al., 2001, Koenigsberg et al., 2002), whereas such stressors were thought to play a less prominent role in bipolar disorder (Malkoff-Schwartz et al., 2000). However, stressful life events are reported to be associated with relapse in bipolar disorder (Aronson and Shukla, 1987, Hammen and Gitlin, 1997). Interpersonal sensitivity has been described in bipolar-II and was found to be significantly higher than in matched patients with unipolar depressive disorder (Benazzi, 2000b). Bipolar disorder is also associated with greater emotional reactivity when compared to healthy controls in an emotional induction task (M'Bailara et al., 2009). Axis-II pathology was not explored in any of these studies, so it is unclear to what extent the presence

of comorbid borderline personality disorder may have accounted for the findings.

Inappropriate or intense anger

Anger is a common feature of borderline personality disorder, with 98.3% reporting chronic anger or frequent angry acts at baseline in the Maclean Study of Adult Development (Zanarini et al., 2007). While anger and irritability are in the diagnostic criteria for mania there is increasing evidence that they are present in all poles of the illness including euthymia. Ballester et al (2014) compared anger and aggression ratings for a group of bipolar subjects over 4 years and compared them to a non-bipolar clinical sample and healthy controls. They found that bipolar subjects had persistently higher scores than clinical and healthy control groups irrespective of mood episode. While scores were significantly higher during mood episodes than in euthymia, the scores were unaffected by polarity of the episode, episode severity, the presence of psychosis and current pharmacological treatment. While no direct comparison of the nature or quality of anger in bipolar disorder compared with borderline personality disorder has been made, it is unlikely to be helpful in distinguishing diagnosis. It is also a much overlooked symptom in bipolar disorder, and may be an important treatment target.

Psychotic features

Psychotic or psychotic-like symptoms are found in both bipolar and borderline personality disorder. They were found to be present in 68% of those diagnosed with borderline personality disorder at initial assessment in the collaborative longitudinal personality disorders study (CLPS) (Zanarini et al., 2013). While they are described as being transient or stress-related in the diagnostic criteria, they were found to persist in 50% of patients at 2-year follow-up. Psychotic symptoms are experienced by about half of those diagnosed with bipolar disorder (Judd et al., 2002, 2003), and can be present in both poles of the illness.

In summary, the phenomenology of borderline personality disorder and bipolar disorder is partially overlapping, but the longitudinal development of the syndromes appears usually to be distinct, at least where a single diagnosis is possible. Unnecessary confusion will inevitably arise if the current symptoms that dominate the clinical assessment are drawn from the domains shown to overlap in Table 1.1, and a determined attempt is not made to establish the course of illness from the patient or a relevant informant.

Do bipolar disorder and borderline personality share the same aetiology?

Any claim that the disorders belong together also requires evidence of a similar aetiology, not just the limited overlap of some symptoms. Moreover, the two

phenotypes could be differently moulded outcomes of related genotypes. The respective aetiologies of the two disorders do appear to be different.

Gender

Borderline personality disorder is more common in women (American Psychiatric Association, 1994), although this widely held belief has been challenged. The NESARC found borderline personality disorder to be equally prevalent in men and women (Grant et al., 2008). Some authors have argued that this relates to clinician bias (that clinicians are more likely to make the diagnosis if the patient is female (Henry and Cohen, 1983)). This argument has largely been discounted (Strain, 2003, Woodward et al., 2009). No individual diagnostic criterion has been found to be more commonly rated in women than men (Davis, 2010). The gender differences are more likely to relate to respective comorbidities associated with gender. Women are more likely to have comorbid mood and anxiety disorder and therefore more likely to seek pharmacotherapy and psychotherapy than men who have greater comorbid substance misuse and are more likely to access rehabilitation services (Sansone and Sansone, 2011). Thus the long held belief that borderline personality disorder is more prevalent in women, may be the result of sampling bias. Bipolar disorder (unlike unipolar disorder) is equally prevalent in men and women although rapid cycling, hypomania and mixed episodes (symptoms common in borderline personality disorder) are more frequently found in women (Diflorio and Jones, 2010).

Heritability

Bipolar disorder has a strong genetic component. Twin studies have demonstrated heritability of .68 to .80 (Goodwin and Jamison, 2007) for bipolar disorder compared to between .37 and .69 in borderline personality disorder (Distel et al., 2008, Kendler et al., 2008, Bornovalova et al., 2009). The prevalence of borderline personality disorder in relatives of probands with borderline personality disorder is 14.1% (Gunderson et al., 2011b) (4.9% for control probands) compared with 10.7% for relatives of bipolar probands (1% for control probands). In borderline personality disorder probands prevalence of bipolar disorder is estimated to be between 0.54% and 4.5% - figures roughly similar to that in the general population (Zanarini et al., 2009, Loranger et al., 1982). However, a twin study of all personality disorders, which explored both genetic and environmental risk factors found that genetic risk factors did not reflect cluster A, B or C typology although environmental risk factors did. This suggests that genetic factors may predispose to personality disorder more broadly while it is environmental factors that differentiate specific clusters (Kendler et al., 2008).

Early abusive experiences

Borderline personality disorder very frequently relates to abusive experiences in childhood, with 80% reporting abuse and 76% reporting neglect during childhood (Herman et al., 1989, Zanarini et al., 1989, Ogata et al., 1990). However, abusive experiences are unlikely to be specific to borderline

personality disorder. In a meta analysis, Fossati et al. (1999) reported the effect size of the association between borderline personality disorder and abusive experiences to be low. The belief that borderline personality disorder relates to early abuse may be a misconception as 80% of those who experience sexual abuse do not develop personality disorder (Paris, 1998), and in an outpatient sample early abuse (physical or sexual) was not found to predict a borderline personality disorder diagnosis (Bierer et al., 2003). The relationship between abuse and borderline personality disorder may be mediated by genetic factors as discordant twin studies suggest that it is inherited vulnerabilities to externalising or internalising disorders that account for the emergence of borderline personality disorder rather than early abusive experiences *per se* (Bornovalova et al., 2013). Early abusive experiences are generally thought to be less common in bipolar disorder. However, reports of abuse in bipolar disorder are significantly higher than in unipolar depressive disorders (UD) (32.4% for bipolar disorder vs 25.1% for UD) (Hyun et al., 2000). Others report that up to half of those with bipolar disorder have experienced abuse during childhood (Garno et al., 2005). However, none of the studies report axis-2 comorbidity so findings may be mediated by the presence of comorbid borderline personality disorder. Early abusive experiences are associated with more severe clinical characteristics in bipolar disorder and this association is most prominently seen in women (Etain et al., 2013).

Do bipolar disorder and borderline personality disorder share the same co-morbidity?

The misuse of drugs and alcohol is common to both disorders. Bipolar disorder is associated with higher rates of lifetime alcohol abuse than any other axis-1 disorder, with just under 50% meeting criteria (Regier et al., 1990, Cassidy et al., 2001). Mania is particularly associated with alcohol abuse / dependence whereas major depressive episodes are not. Lifetime prevalence of alcohol use disorders is similar in borderline personality disorder with 57.3% of respondents in the NESARC study reporting alcohol abuse or dependence (Grant et al., 2008). Drug abuse disorder is also similarly prevalent in both disorders; 36.2% in borderline personality disorder and 41% in bipolar disorder. Determining the relationship between the mood symptoms and onset of alcohol or drug use presents a number of methodological problems. In both diagnoses it seems likely that substances are used to provide some temporary relief from mood symptoms. Both borderline personality disorder and bipolar disorder are associated with high rates of comorbid anxiety disorder 74.2% in borderline personality disorder (Grant et al., 2008) and 74.9% in bipolar disorder (Merikangas et al., 2007), with anxiety symptoms being a common feature of depressive, mixed or manic states (Gibb et al., 2005). Post traumatic stress disorder (PTSD) is commonly associated with borderline personality disorder with 39.2% fulfilling criteria for a lifetime diagnosis compared with 18.9% in bipolar disorder (Merikangas et al., 2007). Rates are considerably higher in females with borderline personality disorder when compared to males (47.2% vs 29.5%, $p < 0.01$). However, the distinction between PTSD and borderline

personality disorder remains controversial as both can be viewed as arising from damage to the attachment system (Zulueta, 2009).

Do bipolar disorder and borderline personality require the same treatments?

The mainstay of treatment in bipolar disorder is medication in the form of mood stabilisers and/or lithium, whereas psychological therapies are the predominant approach in borderline personality disorder. However, bipolar disorder does benefit from psychological intervention (National Collaborating Centre for Mental Health, 2014) and some medications, for example sodium valproate or lamotrigine, have been found to be helpful in borderline personality disorder (Lieb et al., 2010). Overall the use of medication in borderline personality disorder is as much based upon a lack of evidence as evidence of a lack of efficacy, and most of these medications are helpful for specific symptoms rather than reducing the overall severity of the illness. In reality many people with personality disorders are prescribed psychotropic medication (POMH-UK, 2012), and polypharmacy is common. The evidence for long-term psychological treatments in borderline personality disorder is more consistent (Binks et al., 2006). However, many treatments are experimental, and there are relatively few randomised control trials making it difficult to make firm conclusions regarding efficacy or in distinguishing one treatment from another. Similar difficulties are encountered in interpreting the data regarding the use of psychological treatments as an adjunct to medication in bipolar disorder (Beynon et al., 2008), so firm conclusions are difficult to reach. Despite these

uncertainties the need for medication in bipolar disorder is indisputable. While there are no treatments for borderline personality disorder for which there is a clearly defined evidence base, current opinion reflected in national guidelines strongly supports the use of psychological therapies as opposed to pharmacotherapy (Grunze et al., 2010, National Collaborating Centre for Mental Health, 2014). Given the clear differentiation in treatment recommendations for the two disorders, the incorrect diagnosis could lead to patients receiving inadequate or inappropriate treatment.

Do bipolar disorder and borderline personality disorder have the same prognosis?

The best reason for distinguishing the cross-sectional similarities of the two disorders is the counter offered by their different longitudinal course. Bipolar disorder is a relapsing and remitting illness with only 16% achieving recovery (defined as no episode for the past 5 years) and 50% experiencing recurrent episodes over a 40 year follow-up (Angst, 1980). By contrast, borderline personality disorder improves significantly with maturity: 50% achieve recovery in the 10 years following diagnosis, 86% attaining a sustained remission of at least 4 years of whom only 15% experienced a recurrence (Zanarini et al., 2010). Follow-up studies of hospitalised borderline personality disorder cohorts (Plakun et al., 1985, McGlashan, 1986, Paris et al., 1987) also describe an improvement in symptoms particularly in impulsivity and intense unstable relationships. For individuals diagnosed during adolescence the majority remit within 4 years (Biskin et al., 2011), furthermore given that at least some of the

borderline personality disorder symptoms overlap with what might be thought of as normal adolescence this figure may represent an overestimate. The difference in prognosis is so striking that it makes the case for an accurate diagnosis without further argument and has important implications for treatment.

Does neuroimaging distinguish bipolar disorder and borderline personality disorder?

The findings of neuroimaging studies have shown both common and divergent patterns of activation in the lateral and medial prefrontal cortex - areas involved in a wide range of cortical processes including social cognition and emotional regulation. However, few conclusions can be drawn from these findings as there is a paucity of studies where direct comparisons of bipolar disorder and borderline personality disorder have been made. Differences in the brain structure of individuals with bipolar disorder when compared with age-matched individuals with borderline personality disorder were identified by Rossi et al (2012, 2013). Manual tracing reveals that borderline subjects had smaller hippocampal volumes when compared to healthy controls, whereas in bipolar disorder this was only detectable on the right side (Rossi et al., 2012). Surface maps reveal distinct differences in grey matter loss with loss primarily in the subiculum in borderline subjects and in the right dentate area in bipolar subjects. Grey matter volumetric differences and distribution differed significantly between the two disorders (Rossi et al., 2013). Bipolar disorder is associated with reduced grey matter volume compared with healthy controls and this reduction is about twice the reduction seen in borderline personality

disorder. These differences were more diffusely distributed in bipolar disorder involving cortical and subcortical structures, whereas in borderline personality disorder they were confined to fronto-limbic regions. White matter changes were less pronounced than grey matter changes in both groups with clusters specific to each diagnosis with little overlap. While participants in both studies were in receipt of psychotropic medication, the results support the hypothesis that bipolar disorder and borderline personality disorder are separate conditions.

In the only study to employ functional magnetic resonance imaging (fMRI) Malhi et al (2013) used an emotional stroop task to explore fronto-limbic network engagement in the two groups. No significant differences in reaction times or accuracy of responses were found. Both groups were found to display similar patterns of changes in the lateral prefrontal cortex, with a reduction of activity in the left dorsolateral prefrontal cortex and an increase in activity in the right ventrolateral prefrontal cortex but a divergent pattern of activity involving heightened dorsomedial prefrontal cortex in bipolar disorder and diminished amygdala activity borderline personality disorder. The results suggest that the neural substrates of emotional regulation are similar (they both had reduced dorsolateral prefrontal activity suggesting that the ability to exert voluntary control over emotional responses was compromised) but not identical. In a subsequent paper, the authors report resting state data acquired from the same patient cohort (Das et al., 2014). Functional network connectivity was found to be increased in bipolar disorder, whereas it was decreased in borderline personality disorder. The increased connectivity in bipolar disorder specifically involved inferior parietal lobule, temporoparietal junction and superior temporal sulcus (often referred to as the social salience network)-ventromedial prefrontal

cortex and dorsomedial-precuneus coupling. In borderline personality disorder connectivity between the social salience-precuneus and the social salience-right frontoparietal networks was reduced. The authors propose that this suggests impairments in the interaction between the social salience detection system and self-referential processing are present in bipolar disorder whereas borderline personality disorder is associated with impaired interaction between the social salience and emotion regulatory system. These findings are consistent with the clinical presentation of the respective conditions.

The paucity of studies makes it difficult to draw any firm conclusions. Brain imaging studies do provide some very limited insight into how bipolar disorder and borderline personality disorder might be differentiated, as well as a platform for further research.

What is current clinical practice?

The rates of misdiagnosis in bipolar disorder and borderline personality disorder in clinical practice are largely unknown as few studies have sought to explore it systematically. Patients with borderline personality disorder have significantly greater odds of being diagnosed with bipolar disorder compared with psychiatric outpatients who do not have borderline personality disorder although no specific borderline criterion has been found to predict this misdiagnosis (Zimmerman et al., 2010, Ruggero et al., 2010). In a population of psychiatric outpatients who had previously been incorrectly diagnosed with bipolar disorder, 25% were found to have borderline personality disorder when subjected to formal

diagnostic assessment using the SCID-1 and -2 (Zimmerman et al., 2010). However, the misdiagnosis occurs in both directions. Evidence of bipolarity (defined as bipolar-1 or -2) has been found in 44% of patients who had previously been diagnosed with borderline personality disorder (Deltito et al., 2001). This figure rises to 69% if those who had experienced hypomanic switches during antidepressant therapy were included (Deltito et al., 2001). There have also been suggestions that clinical diagnoses do not stand up to the rigor of a diagnostic interview. One study reported that over half of supposed borderline personality disorder participants who had received diagnoses based on clinical assessment did not meet criteria for borderline personality disorder when subjected to a SCID-2 interview (Atre-Vaidya and Hussain, 1999).

Objective approaches have also been criticised as being unable to discriminate effectively between the two diagnoses. The Mood Disorders Questionnaire (MDQ) is a self-report screening questionnaire developed to improve the detection of bipolar disorder (Hirschfeld et al., 2000). In a sample of 480 psychiatric patients those that screened positive on the MDQ were found to be just as likely to have bipolar disorder (23.5%) as borderline personality disorder (27.6%) when diagnosed using the SCID-1 and SCID-2 (Zimmerman et al., 2010). In a further study of individuals with eating disorders the MDQ had similar sensitivity and specificity in identifying bipolar disorder and borderline personality disorder respectively (Nagata et al., 2013). These findings are not wholly surprising given the overlapping symptoms of the two disorders. While the MDQ is not a diagnostic tool, it has been used in some studies as an indication of bipolar experience in young people (Yip et al., 2012, Rock et al., 2010).

Borderline personality disorder is associated with discrepancies between self-reported symptoms and behavioural outcomes (Jacob et al., 2010) and patients with borderline personality disorder tend to exhibit a negative recall bias when compared with healthy controls (Ebner-Priemer et al., 2006). These distortions make the use of any standardised mood questionnaires more difficult.

While it might be reasonable to assume that clinicians are basing their diagnostic differentiation upon the criteria laid out in DSM IV, there is a paucity of evidence to support or refute the application of operationalised diagnostic criteria outside of research settings. Anecdotal evidence suggests that clinicians are often unduly influenced by their subjective reactions to the patient and the range of behaviours they might display in a short period of contact. While a self-report survey of clinicians suggested that they relied on longitudinal observations (Westen, 1997) when considering personality disorder a large observational study of new assessments found that clinicians more frequently diagnosed personality disorder on initial evaluation particularly if given access to answers from the borderline module of the SCID-2 (Zimmerman and Mattia, 1999). There has been a historical reluctance to make the diagnosis of borderline personality disorder as clinicians have judged it untreatable (Lewis and Appleby, 1988), and badly received by patients. In addition, deliberate misdiagnosis may also be chosen in order to justify a particular management strategy, for example the use of low dose antipsychotic medication in borderline personality disorder, or as a means of accessing services where diagnosis serves a gatekeeping function.

There is no doubt that operationalised criteria improve the reliability of diagnoses in research settings, but they are rarely used in clinical practice (Zimmerman et al., 2010). Prototype models for diagnosis have been suggested on the basis that they are more congruent in a clinical setting (Westen et al., 2006). These models involve comparing the characteristics of a patient to a predetermined template. It has been suggested that this approach to the diagnosis of personality disorder is more user friendly and has greater clinical utility (Westen et al., 2006). However, prototypic methods of diagnosis have their limitations. They remain reliant upon clinicians recalling and applying the template. Concerns have been raised that such an approach may lead clinicians to infer symptoms which are not present and that there will be significant variability between clinicians in instances where a presentation less clearly conforms to any given prototype (Maj, 2011). In reality both approaches are open to bias and neither overcomes the issue of shared symptoms in bipolar disorder and borderline personality disorder although the prototypic model does allow for the context in which symptoms occur to be more meaningfully interpreted.

Why is correct diagnosis important?

Accurate diagnosis is central to patient care: It can ensure evidence-based treatment, provide patients with a framework within which to understand their difficulties, allow clinicians to give accurate information about heritability and prognosis, and ensure clear communication of clinical information. At a societal level, diagnoses are used in commissioning healthcare and predicting future

healthcare costs. Finally it is what all General Practitioners expect to receive in letters from psychiatrists (Najim and Loughran, 2012).

Therefore, psychiatric diagnosis matters as a pragmatic tool for communicating about patterns in psychiatric illness. Its strength lies in its reliability, which can be estimated by looking at inter-rater agreement in clinical samples. This can achieve high values (conventionally described with the Kappa statistic) when structured interviews are employed; over 0.9 for bipolar diagnoses (Simpson et al., 2002) and over 0.75 for borderline diagnoses (Zanarini et al., 2002). Such agreement reflects the consistent identification of symptoms or patterns of symptoms. By this activity, a skilled psychiatrist adds value to the patient record. Even if a diagnosis is not possible, the information recorded in letters or notes remains valuable for future assessments, especially in secondary care.

In clinical practice, while it is a standard of care to record assessments and diagnoses in the patient record, there have been few studies exploring how comprehensive psychiatrists actually are when performing diagnostic assessments (First et al., 2004). The recent 'fieldwork trials' for DSM-5 are a rare recent example looking at categorical diagnoses in sequentially recruited rather than highly selected patient samples and *without* structured clinical interviews. Bipolar-I and borderline personality disorder diagnosis showed very good reliability (Kappa 0.75) in some centres but not in others (Regier et al., 2013). Thus, even when diagnosis is under explicit scrutiny, it cannot be assumed agreement will be high.

DSM-5 and ICD-11

The classification and diagnostic criteria for borderline personality disorder in DSM-5 has not changed from that outlined in DSM IV despite radical proposals which included changing classification of all personality disorders to a hybrid model. Requests were made to rename borderline personality disorders as "emotional regulation disorder" or "emotional dysregulation disorder". There was also discussion about changing borderline personality disorder to an Axis-I diagnosis. These proposed changes were rejected by the DSM-5 board, but an alternative hybrid model of personality disorder is included in part III of the manual (see appendix 2). The extent to which this alternative model will be employed in clinical practice remains to be seen.

The proposed changes to the International Classification of Disease volume 11 (ICD-11) classification of personality disorder are far more radical (Tyrer et al., 2011) (see appendix 3). The new classification attempts to address the dimensional nature of personality disturbance. The revisions include a primary classification of personality disorder based on severity alone, and a secondary classification based upon five domains of personality disturbance: asocial/schizoid, dissocial/antisocial, obsessional/anankastic, and emotionally unstable. In addition sub-threshold levels of personality disturbance will also be assigned specific codes. The working group argue that this approach will reduce heterogeneity and that the large number of people showing some form of personality disturbance (Tyrer et al (2011) suggest perhaps the majority) will serve to destigmatise this group of disorders. The ICD-11 proposals have yet to

be approved by the International Advisory Group for the Revision of ICD-10 and will be subject to further approval processes and field testing. Should they be approved, as seems likely, harmonising the ICD and DSM diagnostic classifications will be challenging.

The classification of bipolar disorder has changed in DSM-5 to facilitate earlier detection with greater emphasis on changes in activity and energy as well as mood (American Psychiatric Association, 2013). The criteria for a mixed episode have been removed, and a new identifier “with mixed features” introduced which can apply to both manic/hypomanic and depressive phases. There have also been changes to the conditions for other specified bipolar and related disorders to include individuals that meet all but the symptom duration criterion for hypomania. An anxious distress specifier has also been included. The changes to the description of mixed states provide greater flexibility than those of DSM IV in which criteria for both depression and mania had to be met for at least a week. However, the lower threshold for mixed states will allow admixtures of mood symptoms to be included, and there is a risk that it will be used loosely and be applied far beyond the bipolar spectrum without any prognostic significance or therapeutic benefit. It may also increase the likelihood of misdiagnosis because of its low specificity and imprecise definition (Malhi, 2013).

The proposed changes to bipolar disorder in ICD-11 are less likely to impact significantly upon clinical practice than those for borderline personality disorder

as the diagnostic criteria remain broadly unchanged. Both DSM-5 and ICD-11 classifications for mental disorder are largely based on clinical observation and patients' self-reported symptoms. As such they are rarely informed by recent developments in genetics or neuroscience. This limitation means that while it may be possible to ensure reliability and consistency of diagnosis it may remain difficult to confer validity. A neuroscience-based approach to diagnosis is not yet feasible, but the National Institute for Mental Health Research Domain Criteria (NIMH RDoC) project provides a framework to facilitate progression towards this. The RDoC project intent is to translate rapid progress in basic neurobiological and behavioural research to an improved integrative understanding of psychopathology and the development of new and/or optimally matched treatments for mental disorders (Sanislow et al., 2010). The transdiagnostic approach inherent within the RDoC project could have significant implications for our understanding of the relationship between bipolar disorder and borderline personality disorder particularly, in light of their overlapping diagnostic criteria.

Conclusion

Misdiagnosis between bipolar disorder and borderline personality disorder in either direction can involve longer periods without treatment, greater morbidity and loss of function. Patient expectations regarding treatment success may be unrealistic, and subsequent changes in diagnosis confusing and upsetting. To make the distinction between diagnoses, simple descriptions based upon broad DSM-IV descriptions of current phenomenology will not work. A more probing

approach to the patient experience and the observations of the clinician are required. The development of an empirical basis for more accurate means of establishing the diagnoses of borderline personality disorder and bipolar disorder is urgently needed in order to enable early identification and individuation of illness and the associated advantages it conveys.

At present little is known about current diagnostic practice in clinical settings. In the following two chapters I report three linked studies with the aim of understanding diagnostic practice in the assessment of patients presenting with mood instability in the UK. Chapter two explores clinicians' experiences of distinguishing bipolar disorder and borderline personality disorder and their knowledge of the diagnostic criteria. Chapter three describes direct observations of clinical practice. Chapters four to seven describe results from a battery of cognitive tests designed to distinguish bipolar disorder and borderline personality disorder. In chapter four the clinical characteristics of twenty participants with borderline personality disorder, twenty participants with bipolar disorder and twenty healthy controls who took part in the laboratory study are described. In chapter five I explore how social behaviour measured in a laboratory setting may distinguish borderline personality disorder and bipolar disorder. In chapter six I investigate how the role of loss and reward in decision making differs in borderline personality disorder and bipolar disorder, and chapter seven I describe findings from a simple choice reaction test. Overall conclusions and future research directions are described in chapter eight.

2. THE CLINICIAN'S PERSPECTIVE

Little is known about clinicians' perceptions of the diagnostic challenges posed by patients where borderline personality disorder or bipolar disorder are likely differential diagnoses. Anecdotal evidence suggests that it is a common source of uncertainty and disagreement among clinicians.

I conducted a qualitative study of clinicians working in the National Health Service (NHS) with the aim of gaining a coherent understanding of the challenges they encounter when distinguishing bipolar disorder and borderline personality disorder. Qualitative methods are particularly appropriate because they are flexible, grounded in the individual experience, and because we know little about clinicians' experience of making these diagnoses. A questionnaire was developed based upon the themes generated in the qualitative interviews. The questionnaire tested the theoretical knowledge and practical experience of a large number of members of the Royal College of Psychiatrists.

QUALITATIVE STUDY

Method

This study was funded by an NIHR Research for Patient Benefit (RfPB) grant (PG-PB-0909-19070). Ethical approval for the study was obtained from Oxfordshire REC A (11/H0604/8).

Study Design

This qualitative study used clinician interview data that were collected as part of a larger project conducted jointly with Dr Bilderbeck, Prof Goodwin and Dr

Price, which involved clinician interviews, patient interviews, analysis of case notes and observation of diagnostic assessments.

Data Sources

Participants were 32 mental health professionals recruited from secondary mental health services in Oxfordshire and Buckinghamshire. This included 7 community mental health teams (CMHTs), a specialist Mood Disorders Clinic, and a specialist personality disorder service. The majority of participating clinicians were doctors (N=26). The remaining participants were psychiatric nurses and social workers. Participants were clinicians who had agreed to assess a patient referred with mood instability. Purposive sampling was used to ensure a range of ages, professional backgrounds and geographical locations. Unlike sampling in quantitative studies where the goal is to randomly sample a populations with the intention of making inferences from that sample to the population in general, purposive sampling focuses on particular characteristics of a population that are of interest.

Inclusion criteria included being fully qualified in their discipline, fluent in spoken and written English and having a clinical role in the provision of frontline NHS mental health services. Written informed consent was obtained from all participants (both clinicians and patients), including for audio-recording and anonymous quotations.

I was responsible for securing the project funding, writing the study protocol, analysing the qualitative and quantitative data from clinicians and the analysis of the recorded assessments (see chapter 3). Study recruitment, data collection

and interview transcription was done jointly with Dr Bilderbeck. The study design and topic schedule were devised with Dr Price and Professor Goodwin.

Data gathering

Demographic data were gathered from all participants, including: age, gender, qualifications, and any specialist experience or training in bipolar or borderline personality disorder (see table 2.1). In the majority of cases (N=24) patient assessments were also observed and/or audio recorded.

	Male	Female	Total
N	16	16	32
Age (yrs.)	39.1	39.4	39.3
Medical qualification	16	10	26
MRCPPsych	15	8	23
CMHT	9	5	14
Specialist mood disorders clinic	2	3	5
Self-harm team	0	2	2
Psychotherapy/Therapeutic community	0	4	4
Specialist training:			
Bipolar	1	1	2
Borderline	1	3	4
Both	0	3	3

Table 2.1 Characteristics of 32 clinicians who took part in the qualitative study

Most participants were working in community mental teams. A small proportion of participants were from more specialist settings for the assessment and

treatment of mood disorders (specialist mood disorders clinic) and personality disorder (psychotherapy/therapeutic community).

Interviews

Clinician interviews were conducted using a topic schedule (see appendix 4). In all instances these interviews were audio-recorded. Clinicians were asked to reflect on the assessment that had been observed, to describe their experience of distinguishing bipolar disorder and borderline personality disorder and the factors that influence them in making this distinction. More specific questions were added to the topic schedule as our understanding of the views of clinicians increased. Interviews varied in length from 20 to 100 minutes. The majority of interviews took place in a private room within the mental health team base as soon as was practicable after the assessment. Some participating clinicians completed multiple interviews in instances where patients had multiple assessments or where clinicians assessed more than one patient meeting the inclusion criteria resulting in a total of 38 interviews.

Data Analysis

Quantitative data were summarised using standard statistical approaches; qualitative data coding, management and analysis were conducted using Nvivo software (QSR International). Semi-structured interviews were conducted as part of an on-going and iterative process of data collection and analysis. Audiotaped interviews were transcribed, reviewed, and uploaded to Nvivo.

Identifying information was removed from transcripts to preserve anonymity. Qualitative analysis used a framework technique (Ritchie and Spencer 1994). Participant data were interpreted and summarised. Codes comprised of similar information were merged, leading to a framework of specific phenomena that appeared increasingly likely to describe patients' experience of assessment. The study team met regularly to discuss the findings and refine the emerging framework. Data gathering ceased when understanding of the experience of clinicians in assessing and diagnosing in patients with mood instability was no longer being advanced. To reduce researcher bias, we discussed and maintained an awareness of preconceptions (facilitated by interviewer note-keeping and memos) and constantly linked the emerging thematic framework to clinician-derived data.

Results

Clinician perception of the problem. (Box 2.1)

Most clinicians agreed that distinguishing between the two diagnoses could be challenging at times. Overlap in diagnostic criteria between bipolar disorder and borderline personality disorder was raised by many clinicians particularly in regard to mood instability. The need to rely on self-reported mood symptoms and the context in which these symptoms were reported were highlighted by most as particularly challenging. Inaccurate retrospective recall of mood states was regarded as particular problem. Chaotic lifestyles, including the use of illicit

drugs, were reported as additional challenges, as were the difficulties of conducting diagnostic assessments in crisis situations.

“The main problem is that uh people with emotional unstable personality disorder do experience significant mood swings and they describe their mood as unstable, and uh therefore I mean by definition it becomes a real issue about who is within the borderline spectrum versus who is in the bipolar spectrum.” (CMHT psychiatrist 05)*

“I challenge anyone to be able to say what their mood’s like reliable over that period of time. So there are real problems in retrospective diagnosis (Mood disorders specialist 01)

“it gets difficult is when people present with quite extreme behaviours, um people with bipolar can present as very agitated, sometimes they present with sort of psychotic or quasi-psychotic symptoms, and they I think they tend to be the ones where it’s difficult to differentiate” (CMHT psychiatrist 17)

“my experience is that there’s a significant subset of people with bipolar disorder who exhibit a lot of chaotic lifestyle, some symptoms that would fit within kind of more personality aspects and this kind of wondering about certain kind of personality kind of features might predispose you towards it.” (CMHT psychiatrist 25)

“So she’s on holiday with her friends, they’re going to a nightclub, there’s drink involved, to what extent is it a reflection of the illness, and to what extent is it the outside, what one might expect from someone going to a, an Ibiza nightclub or - I don’t know” (Mood disorders specialist 02)

*(numbers following participant description denote participant number)

Box 2.1 Clinician perception of the problem

Utility of distinguishing the diagnoses (Box 2.2).

Many clinicians questioned the validity of the borderline personality diagnosis, and felt that determining the presence or absence of an axis 1 disorder was more important because this was their primary focus for treatment. Some clinicians queried the usefulness of distinguishing the diagnoses and a few clinicians suggested that bipolar disorder and borderline personality disorder were on a continuum.

“My feeling is it is not that clear cut between them is like um spectrum” (CMHT psychiatrist 07)

“I see bipolar affective disorder and borderline PD as being on a sort of continuum..... both groups would be using sort of manic defences at some point.” (Psychiatrist in psychotherapy 06)

“I don't think that the borderline personality disorder is, it should be a separate diagnosis I think it exists on a spectrum of various disorders”. (CMHT psychiatrist 27)

“to some extent, being able to understand their problem with the diagnostic category can be helpful, but PD categories are so useless in many ways” (RMN/Group analyst 08)

“I think fundamentally I think the diagnoses of personality disorder mostly lack validity. They're not clear-cut discrete entities. You don't either have it or don't have it. There aren't clear cut-offs of when you have a personality disorder and when you don't have a personality disorder” (CMHT psychiatrist 18).

“my initial attempt is to make the axis 1 diagnosis, as far as I'm concerned if the person meets criteria for bipolar disorder then that would put a target at my therapeutic endeavours. Whether or not I think they've got a personality disorder as well “ (Mood disorders specialist 01)

Box 2.2 Utility of distinguishing the diagnosis

Use of the diagnostic criteria (Box 2.3)

While most clinicians stated that the diagnostic features were helpful in distinguishing the two diagnoses, the lack of specificity of many of the presenting features was felt to represent a clinical challenge. Most clinicians felt that limiting assessment to the diagnostic checklists would inevitably lead to incorrect diagnoses being made, and they preferred to place greater weight on clinical judgement and impressionistic approaches.

“if you go to someone who's got borderline-type problems, and you just try to find out if they've got bipolar - have had a hypomanic episode, and you just ask your questions in that way, you'd be very likely to erroneously conclude that they have had a hypomanic episode.” (CMHT psychiatrist 25)

“So you could say well look this is, this will if you just take what she says at face value she ticks a lot of the boxes for a mania but um I think I wasn't convinced that that was a mania I didn't think that that was actually what happened from the description that she gave to me. Not that she was lying” (CMHT Psychiatrist 16)

“you can refer to diagnostic criteria, particularly with bipolar disorder, but a large part of it is about a more difficult to pin down impression which is formed.” (CMHT Psychiatrist 03)

“So I think if you're someone who goes, what do I feel this patient is presenting to me with? Or you're someone who goes well, what boxes am I ticking, I think that that then leads you down two different routes in terms of thinking about diagnosis” (CMHT psychiatrist 25)”

“they are helpful, uh and they give you some sense of direction, um uh but sometimes I um I use I need to use my clinical judgement rather than uh the diagnostic criteria to diagnose the borderline personality disorder” (CMHT psychiatrist 26)

Box 2.3 Use of the diagnostic criteria

Other features distinguishing the diagnoses (Box 2.4).

Many clinicians felt that the nature of the clinician-patient relationship during the clinical assessment was an important influence on their diagnostic decision making. This was particularly the case with borderline personality disorder, where hostility and assuming a childlike relational position were felt to be indicative. Specific historical factors, such as early abusive experiences and attachment difficulties were frequently reported as more relevant to a borderline diagnosis, and an absence of these features was often cited as grounds for not making the diagnosis.

“...severe difficulties during her teenage years and so there's abuse as well,..... it will tend to favour borderline diagnosis” (CMHT psychiatrist 04)

“if they're problems have been long-term and chronic and you know and you can clearly go back to difficulties in upbringing and attachment I think the diagnosis of personality problems becomes much more likely”(CMHT psychiatrist 18)

“he is impulsive and, but I don't, didn't pick up any true borderline sort of traits. He isn't self-harming, he um seems to have come from quite a caring, stable-type background” (Specialty doctor 15)

“how the person comes across to me, in the interview – it's not all historical. I will look at the way they're reacting to me, do I feel that they're being straight with me, is there an air of trickiness or hostility about them “ (Mood disorders specialist 01)

“the patient takes a more childlike position and you, you have to make the decisions about everything on this person's care. That's not the classic interaction I get with people with hypomania. Or mania. They tend to be you know “I know everything” and sort of a bit more you get a far more sort of at times the – you get anger, bravado, and sort of uh you know ‘you know nothing”” (CMHT psychiatrist 05)

“A bipolar person who has no borderline aspects has basic trust. Um, unless they're in the middle of an episode and they're psychotic or their thinking is distorted. They have a basic idea that you're a healthcare professional who's trying to help them with an illness that they are suffering. And somebody who is borderline does not necessarily have that basic idea at all.” (Psychiatrist in psychotherapy 06)

“again this is not within the sort of diagnostic sort of DSM or ICD-10 criteria but something that I find useful is the reactions of the environment towards people and sort of the way people uh either the GP or the family and the way they kind of respond to the individual patient that is referred and then how us as professionals also we kind of interact with this particular patient.”(CMHT psychiatrist 05)

Box 2.4 Other features distinguishing the diagnoses

Other non-clinical factors influencing diagnosis (Box 2.5).

Several factors not relating directly to the clinical presentation or management were cited as influencing diagnostic decisions. These included factors specific to the assessing clinician and systemic factors related to healthcare targets and funding. A lack of knowledge about the management of the two disorders was highlighted by some clinicians as a reason to err on the side of a borderline diagnosis as this was perceived as a means by which clinicians could discharge patients on the basis that they were untreatable. Other clinicians viewed borderline personality disorder as a diagnosis which was used when patients' difficulties did not conform to any specific mood disorder. Pragmatic factors such as the time pressures placed upon clinicians and the increasing use of diagnosis to determine cost and access to care were viewed as important external pressures influencing diagnosis.

“they’re actually saying I feel this person has difficulties that probably don’t fit with any kind of affective illness framework, but they don’t feel very confident in dealing with that, “(CMHT psychiatrist 25)

“there is a sort of lack of incentive for people to make a diagnosis of bipolar disorder if they don’t feel they’re comfortable with what to do about it. Ah, whereas a diagnosis of borderline personality disorder kinda solves the problem really because they’re not going to do anything for it....people don’t like to be manipulatedan exclusive diagnosis of personality disorder is quite a good way of saying I don’t want anything to do with this patient. (Mood disorders specialist 01)”

“....in a busy outpatient clinic you don’t have time. So my consultant will tell please discharge her back to the GP. I know she will say that because she knows how busy and I am and she knows we cannot have the luxury to see patients without active problems, problems happening here and now for more than a couple of times” (CMHT psychiatrist 29)

“I think people clinically start to work in different ways.....I think around that, the system has investments in research, in financial interests, in simplicity for treatment, in the labelling of people..... its categories and its boxes and its money.....pushes clinicians into not seeing the individual, seeing the category, and I think it is hugely detrimental it’s partly how much money is around all of this, means that the patient sitting in the room is not getting an unbiased diagnosis..... borderline personality disorder..... it often means in some CMHTs, not all, that it is seen as or it becomes a reason not to see the person,” (Psychiatrist in psychotherapy 06)

“unlike in the States or other countries where you get paid per treatment given, or diagnosis, or clinical activity, in this country you just get paid regardless of how much you’re doing, there’s no incentive therefore to over diagnose or over treat. Which is a good thing but on the other hand there is an incentive to underdiagnose and undertreat. “(Mood disorders specialist 01)

Box 2.5 Other non-clinical factors influencing choice of diagnosis

Stigma (Box 2.6)

The perceived stigma associated with a borderline diagnosis was also cited as a reason to avoid giving patients this diagnosis. By contrast, bipolar disorder was seen by clinicians as a much more acceptable diagnosis and they believed this was usually the diagnosis sought by the patient, even if the patient's presentation was more likely to represent borderline personality disorder.

"Nobody welcomes.....a diagnosis of personality disorder....unlike bipolar disorder it carries more stigma....so it does feel like a much more judgemental diagnosis....the person sort of has a different response to be given an illness diagnosis versus something that feels like a moral judgement" (Psychiatrist in psychotherapy 06)

"bipolar is a more acceptable diagnosis to have than borderline personality disorder and I think um partly that's our fault as mental health professionals that we can be quite pejorative about personality disorder" (GP trainee 23)

I think that the diagnosis of personality disorder often seems like an excuse for sort of therapeutic nihilism, so you know nothing, it's felt that well we can do nothing to help this person and so let's you know let's just leave them. (CMHT psychiatrist 24)

"I'm not saying bipolar doesn't exist. Clearly, you know, we think it does. Um, I think that a diagnosis of bipolar disorder or being a manic depressive is somewhat more romantic and acceptable, you know because along with it goes creativity, eccentricity of a particular kind, that's kind of acceptable, whereas being a PD, or a borderline, doesn't carry the same kind of strokes." (RMN/Group analyst 08)

Box 2.6 Stigma

CLINICIAN SURVEY

Method

An online survey of psychiatrists was conducted, which explored clinicians' knowledge and use of diagnostic criteria when distinguishing bipolar disorder and borderline personality disorder. It focussed on clinicians' views of the assessment and diagnosis of patients who may have bipolar disorder and/or borderline personality disorder as well as the factors deemed to influence these diagnostic decisions. The majority of survey items used a 5-point Likert-type scale and there were several opportunities for respondents to clarify or expand on the responses they had made in free text (see appendix 5). The survey was based upon the themes that were identified in the qualitative interviews. The questions were drafted by the study team, who met regularly to discuss and amend its content. It was then piloted on two of the clinician participants from the qualitative study before the final draft was agreed.

The survey was hosted online using Limesurvey ([www. Limesurvey.org](http://www.Limesurvey.org)) between September and November 2012. Email invitations were sent out to 8,000 members of the Royal College of Psychiatrists (and 12,000 members of Royal College of Nursing, data not shown) on behalf of the research team. Responses were received from 648 members of the Royal College of Psychiatrists which was a response rate of 8.1%.

Statistical Analysis

Statistical analysis was carried out using SPSS v. 20 for Windows (SPSS Inc, 2007). Data were analysed using univariate analyses with between-subjects factors of gender and clinician grade. Non-parametric chi-squared tests were used in analysis of categorical data. Free text responses were coded as themes emerged.

Results

648 responses were received (response rate of 8.1%) of which 546 (84.3%) were completed in full. The majority of respondents were consultant-grade psychiatrists (68.1%). The remaining were staff grade (7.1%), associate specialist (3.1%) and trainee (21.7%) doctors. The responses were plotted cumulatively over time and converged strongly and stably on the proportions described below (see appendix 6).

Most respondents (71.4%) reported that differentiating between bipolar disorder and borderline personality disorder formed part of their clinical practice (defined as 5% of their case load or more). For a small proportion (6.4%) this formed more than half of their workload. The majority of doctors reported feeling confident in making this discrimination (74.2%); only 1.7% reported feeling not at all confident. A greater proportion of doctors in consultant grades were confident about distinguishing the diagnoses than those in non-consultant grades (79.3% vs 64.4% $\chi^2=16.90$, $p<0.001$). Fifty percent of respondents indicated that distinguishing bipolar disorder and borderline personality disorder

was a source of disagreement in clinical practice with just 2% reporting that this was never the case.

Respondents broadly identified the DSM-IV diagnostic features of the two disorders with the factors they used to distinguish bipolar disorder and borderline personality disorder. Factors which overlap in the diagnostic criteria (impulsivity and affective instability) were correctly viewed as less indicative. Historical factors were also recorded as important in guiding diagnostic decisions, with more than 50% of respondents endorsing early life trauma as strongly or very strongly indicative of borderline personality disorder compared with 7% for bipolar disorder. Forty-eight percent endorsed a positive family history as being strongly or very strongly indicative of bipolar disorder compared with 12% for borderline personality disorder.

Free text responses

Free text responses regarding diagnostic features were received from 97/648 in the case of borderline personality disorder and 167/648 in the case of bipolar disorder. In bipolar disorder half of respondents highlighted the need to focus on obtaining a clear history while 23% highlighted the role of interpersonal dysfunction in identifying borderline personality disorder. For bipolar disorder, 38% highlighted the need to focus on mood changes particularly the presence of elated mood, and a further 10% mentioned the need to identify inter-episode euthymia. The majority of the remaining free text responses were clarifying

answers given previously or to make explicit comments about the setting in which the clinician was working (and in one case to criticize the study).

Use and utility of the diagnostic criteria

There was modest agreement that the diagnostic criteria correlated with their clinical observations of bipolar disorder and borderline personality disorder: 30% were neutral or did not agree that the diagnostic criteria correlated with their clinical observations of bipolar disorder compared with 35% for borderline personality disorder.

Respondents reported a preference for using diagnostic criteria compared with an impressionistic approach. However, impressionistic approaches were endorsed more strongly for borderline personality disorder than bipolar disorder with 24% compared with 13% agreeing that this was their chosen approach. Respondents were equally likely to consult a third party, with 87% vs 82% (for bipolar disorder and borderline personality disorder respectively) consulting a third party in at least half of their assessments.

Overall, most psychiatrists did not view bipolar disorder and borderline personality disorder as being part of the same illness spectrum (71% expressed that this was not the case). Comorbid diagnoses of borderline personality disorder and bipolar disorder were made infrequently, with just 5% endorsing this as a frequent occurrence.

Discussion

To my knowledge this is the first study to explore clinicians' views and experience of distinguishing bipolar disorder and borderline personality disorder.

Clinician perception of the problem

There was broad agreement in both the qualitative and questionnaire studies that the two diagnoses can be difficult to distinguish from one another. Many clinicians expressed the view that the diagnostic criteria did not necessarily assist diagnostic differentiation with some clinicians suggesting that approaches that rely on diagnostic criteria alone would lead to incorrect diagnosis.

The rates of misdiagnosis in bipolar disorder and borderline personality disorder in clinical practice are largely unknown as few studies have sought to explore it systematically. Patients with borderline personality disorder have significantly greater odds of being diagnosed with bipolar disorder compared with psychiatric outpatients who do not have borderline personality disorder although no specific borderline criterion has been found to predict this misdiagnosis (Zimmerman et al., 2010). Evidence of bipolarity (defined as bipolar-1 or -2) has been found in 44% of patients who had previously been diagnosed with borderline personality disorder (Deltito et al., 2001). There have also been suggestions that clinical diagnoses do not stand up to the rigor of a diagnostic interview with one study reporting that over half of supposed borderline personality disorder participants who had received diagnoses based on clinical assessment did not meet criteria for borderline personality disorder when subjected to a SCID-2 interview (Atre-Vaidya and Hussain, 1999).

A third of respondents in the questionnaire study thought diagnostic criteria failed to correlate with the clinical phenomena in borderline personality disorder and bipolar disorder. In both studies clinicians cited early life experiences, attachment difficulties and the nature of the clinical interaction to be equally as relevant as the diagnostic criteria themselves.

The suggestion by some clinicians that the diagnostic criteria are unhelpful in aiding distinction of bipolar disorder and borderline personality disorder is perhaps because they misread the episodic symptoms of bipolar disorder as being a function of their character. The key clinical feature of borderline personality disorder is its pervasive pattern of difficulties commencing in early adulthood which are present in a variety of contexts.

The majority of practising psychiatrists maintain that a diagnostic system based upon clinical descriptions is more useful than a list of operationalized criteria (Marshall et al., 2001, Pinninti et al., 2003). There is no doubt that operationalized criteria improve the reliability of diagnoses in research settings but they are rarely used in clinical practice. The preference of clinicians for impressionistic approaches raises interesting questions regarding the basis upon which their impressions are formed, the utility of diagnostic labels to inform treatment and communication and their medico legal defensibility. The observation that the nature of the interaction with the patient was important is one supported by attachment theories of personality disorder. However, there is

no clear evidence base that such clinical observations are reliable in establishing diagnosis and there is clearly the possibility that clinicians are unduly influenced by their subjective reactions to a patient and the range of behaviours that they display during the assessment appointment.

Other factors

In both studies, clinicians cited a number of other clinical factors that they felt were relevant to the diagnostic differentiation. Early abusive experiences and family history were commonly mentioned. While 80% of those with borderline personality disorder report abuse and 75% report neglect during childhood (Zanarini et al., 1989), approximately half of those with bipolar disorder will also have experienced abuse during childhood (Garno et al., 2005) and early abusive experiences are generally quite common in psychiatric cohorts. The implicit assumption that borderline personality disorder has no genetic basis is also incorrect because heritability is estimated to be between 37 and 69% (Zanarini et al., 2004, Distel et al., 2008, Kendler et al., 2008) and the prevalence of borderline personality disorder in first degree relative is 14.1% (Gunderson et al., 2011b).

External factors

The role of the external factors such as time, finance and discharge from CMHTs is concerning. Payment by results has a number of unintended consequences with incentives to up-code (i.e. for providers to select an unnecessary diagnosis or the most expensive treatment for patients). There is also an incentive to explicitly avoid high severity patients, and this is particularly likely to be the case in diagnostic groups where it is possible to manipulate treatment thresholds or where a significant degree of clinical discretion exists (Miraldo et al., 2006) such as borderline personality disorder.

Stigma

The stigma associated with mental illness is a long standing issue and while it is associated with most diagnoses, it is a particular issue for personality disorder which is often viewed as being a non-biological illness (Paris, 2007). By contrast, recent celebrity publicity surrounding bipolar disorder has led to an increase in self-diagnosis possibly because of the implicit association of bipolar disorder with celebrity status and creativity (Chan and Sireling, 2010). However, avoiding diagnosis because of concerns about stigma only serves to deny patients access to appropriate treatment and an accurate understanding of their illness.

Limitations

The sample of clinicians in the qualitative study was purposively sampled to ensure that I was able to reflect a number of different contexts and geographical spread. The male gender bias in the sample reflects local gender ratios in more senior clinical staff. While, clinicians self-selected in to the study, all those that we initially approached agreed to participate. The reason for non participation following an agreement to do so was that no referrals relevant to the study were made to that clinician during the study period (N=1). Specialist services for the diagnosis and treatment of bipolar disorder are available locally but this is also the case for personality disorder so I do not think that the views expressed here were polarised towards one diagnosis or another on this basis. The consistency of the responses in the questionnaire study with the initial qualitative study findings suggest that the results presented here are likely to be representative of British psychiatrists more widely.

The response rate for the questionnaire study was relatively low which raises the possibility of significant respondent bias. However, the data converged upon the findings presented here within the first 50 responses suggesting that the findings are likely to be representative of more widely held views (see appendix 6).

3. WHAT CLINICIANS DO IN PRACTICE

The confidence of psychiatrists, their awareness of diagnostic controversy in distinguishing bipolar disorder and borderline personality disorder, and their endorsement of relevant symptoms for making the correct diagnosis have been described in Chapter 2. This might predict that the difficulties in differentiating bipolar disorder and borderline personality disorder relate to the overlap in diagnostic criteria or to perfunctory assessments, rather than a lack of knowledge per se. While it is standard practice to keep written records of assessments and diagnoses in the patient record, there have been few studies of how comprehensive psychiatrists are when performing diagnostic assessments (First et al., 2004). Temporal stability of clinical diagnoses is generally poor. In outpatient settings prospective consistency has been found to be 50.6% for bipolar disorder but just 35.6% for personality disorder (Baca-Garcia et al., 2007).

I conducted a detailed study of the diagnostic assessment process in local NHS psychiatric teams who contributed to the qualitative data in Chapter 2.

Method

This work was funded by the Research for Patient Benefit programme (PG-PB-0909-19070). Ethical approval for the study was obtained from Oxfordshire REC A (11/H0604/8).

Data sources

Participants were 20 of the 26 psychiatrists who participated in the qualitative study. The six who did not take part did not consent to being observed. A subsample of fifteen clinicians agreed to have assessments audio recorded. The remaining 25% were not recorded because of technological issues (N=2) or because the patient did not consent (N=3). Written and informed consent was obtained from all participants as well as from their patients. Both clinicians and patients gave consent for us to access electronic patient records.

Diagnostic criteria and diagnoses

GP letters and assessment recordings were analysed to see to what extent the diagnostic criteria were reported. I used a checklist of the symptoms for bipolar disorder and borderline personality disorder as outlined in DSM-IV-TR. I also sought to cluster symptoms for each case to establish whether enough symptoms were explored to warrant the inclusion or exclusion of a specific diagnosis of bipolar disorder or borderline personality disorder. Clinical diagnoses were obtained from the letters sent back to GPs following assessment.

Research diagnoses were generated using OPCRIT + (Rucker et al., 2011). OPCRIT (Operational CRITeria) is a diagnostic system that automates the generation of putative diagnoses using a checklist constructed from the major psychiatric diagnostic classifications. Clinical data derived from patient assessments are entered into the OPCRIT computer programme which

generates diagnoses. It has been used in a wide number of clinical epidemiological and biological research settings (Rucker et al., 2011, Van Os et al., 1999, Azevedo et al., 1999). The OPCRIT checklist is designed for trained clinicians extracting information from interviews, case records and other sources. It has been shown to have good reliability when used by different raters. Data were gathered from all available sources including the GP letter, assessment recordings, assessment letter and any other information recorded in the case notes.

Results

Assessment study

All 30 patient participants were referred from primary care for assessment. The most common reason for referral was for the assessment of possible bipolar disorder (N=21). Two were referred for the assessment of chronic depression and mood instability, one with psychotic depression and possible bipolar disorder, and six contained no specific request but mentioned mood instability. The majority of these referrals were made to CMHTs (93%). A further two participants were assessed at the specialist mood disorders clinic.

Referral Letters

All but one referral letter mentioned low mood (29/30; 97%). Other depressive symptoms were much less consistently described. The presence or absence of features of mania / hypomania, or borderline personality disorder, were less frequently reported, with elation being mentioned in 67%, and affective instability in 50% of cases.

Assessors

The majority of assessing clinicians (17/20) had membership of the Royal College of Psychiatrists (MRCPsych): the standard exam for those training in psychiatry) indicating that the majority of participants had at least 3 years of experience and had received postgraduate training in psychiatry (Table 3.1).

Clinician Characteristics	Total sample N (%)	Sample where assessments were recorded N (%)
GENDER		
Male	14 (70.0)	11 (73.3)
Female	6 (30.0)	4 (26.7)
GRADE		
Consultant	5 (23.8)	4 (26.7)
Specialty Trainee	14 (71.4)	10 (66.7)
Staff grade	1 (4.7)	1 (6.7)
Member of RCPsych	17 (85.0)	12 (80.0)
SETTING		
CMHT	18 (85.7)	15 (100)
Mood disorders clinic	2 (9.6)	0 (0)

Table 3.1 Characteristics of assessing clinicians

Assessment audio-recordings

Eighteen patient assessments were recorded, involving 15 clinicians all of whom were working in CMHTs. The majority of assessed patients were female (21/30) with mean age ($\pm$ SEM) of 34 ($\pm$ 2) and 33 ($\pm$ 3) for females and males respectively.

The numbers of symptoms explicitly covered at interview are shown in Table 3.2. Overall, depressive symptoms were the most thoroughly assessed with the exception of feelings of worthlessness and psychomotor agitation/retardation, which were rarely explored (agitation 2/30 and retardation 1/30 assessments). For each individual case an average of 5 symptoms were explored (of a

possible 9). In 61% cases an adequate number of criteria were assessed to affirm the presence of a diagnosis according to DSM-IV-TR.

Manic symptoms were less likely to be explored than depressive symptoms. In 20% of cases elevated mood was not addressed at all (Table 3.2). The average number of manic symptoms reviewed at assessment was 4.1 (of a possible 8), and only in 38% of cases were an adequate number of symptoms explored to affirm the presence of the diagnosis.

Borderline symptoms were rarely explored. An average of 2.9 symptoms were explored in each assessment, and only in 4 cases (22%) were an adequate number of symptoms explored to affirm the diagnosis. In just two cases (11%) were an adequate number of symptoms explored for depression, mania and borderline personality disorder in the same assessment.

Depression	Number of assessments in which symptom was explored.
depressed mood	28/30
markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day	20/30
significant weight loss when not dieting or weight gain or decrease or increase in appetite nearly every day.	Poor appetite 21/30 Weight loss 8/30 Increased appetite 10/30 Weight gain 8/30
insomnia or hypersomnia nearly every day	Initial insomnia 14/30 Middle insomnia 10/30 Early morning waking 6/30 Hypersomnia 21/30
psychomotor agitation or retardation nearly every day (observable by others)	Agitation 2/30 Retardation 1/30
fatigue or loss of energy nearly every day	23/30
feelings of worthlessness or excessive or inappropriate guilt nearly every day	22/30
diminished ability to think or concentrate, or indecisiveness, nearly every day.	15/30
recurrent thoughts of death, recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide	27/30

Mania / Hypomania	Number of assessments in which symptom was explored.
abnormally and persistently elevated, expansive, or irritable mood, lasting at least 1 week (or hospitalization) for mania, or 4 days for hypomania, clearly different from the non-depressed mood.	Elevated mood 17/30 Irritable mood 16/30
inflated self-esteem or grandiosity	26/30
decreased need for sleep (e.g., feels rested after only 3 hours of sleep)	13/30
more talkative than usual or pressure to keep talking	6/30
flight of ideas or subjective experience that thoughts are racing	7/30
distractibility (i.e., attention too easily drawn to unimportant or irrelevant external stimuli)	1/30
increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation	8/30
excessive involvement in pleasurable activities that have a high potential for painful consequences	9/30

Table 3.2. Proportion of depressive and manic symptoms recorded when all sources examined

The findings may be best understood by reference to the summary spidergrams in Figure 3.1.1-3 showing the findings for the key symptoms of borderline personality disorder, mania and depression.

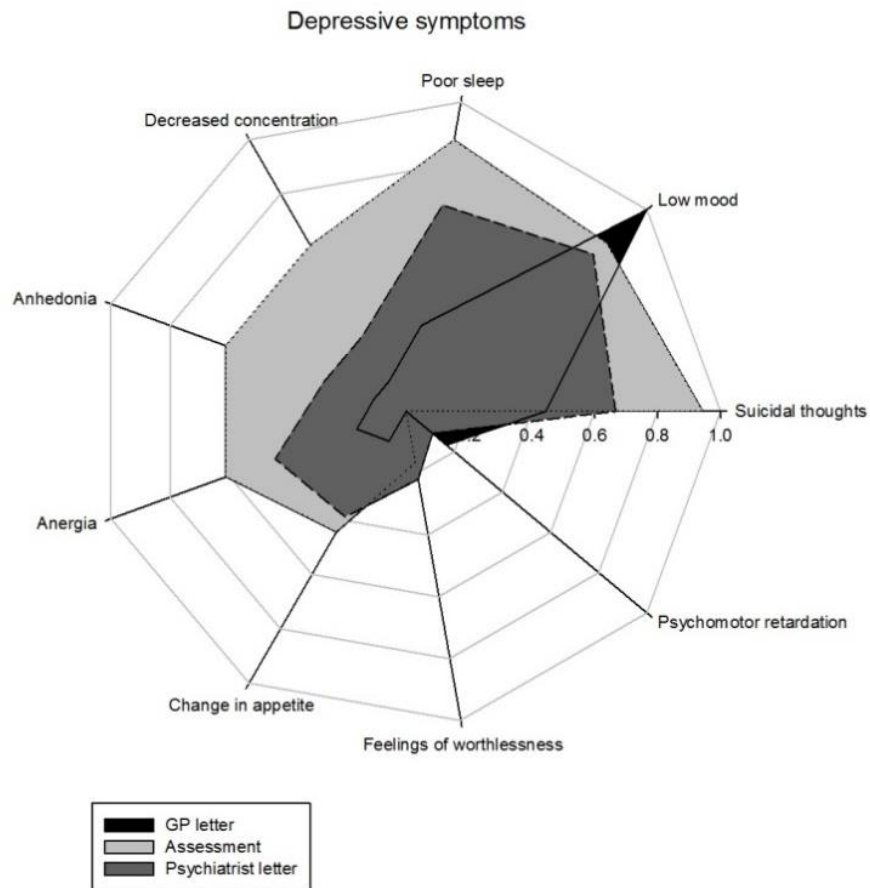


Fig 3.1.1 Proportion of diagnostic criteria for depression included in GP referral letters, assessment and psychiatrist letters.

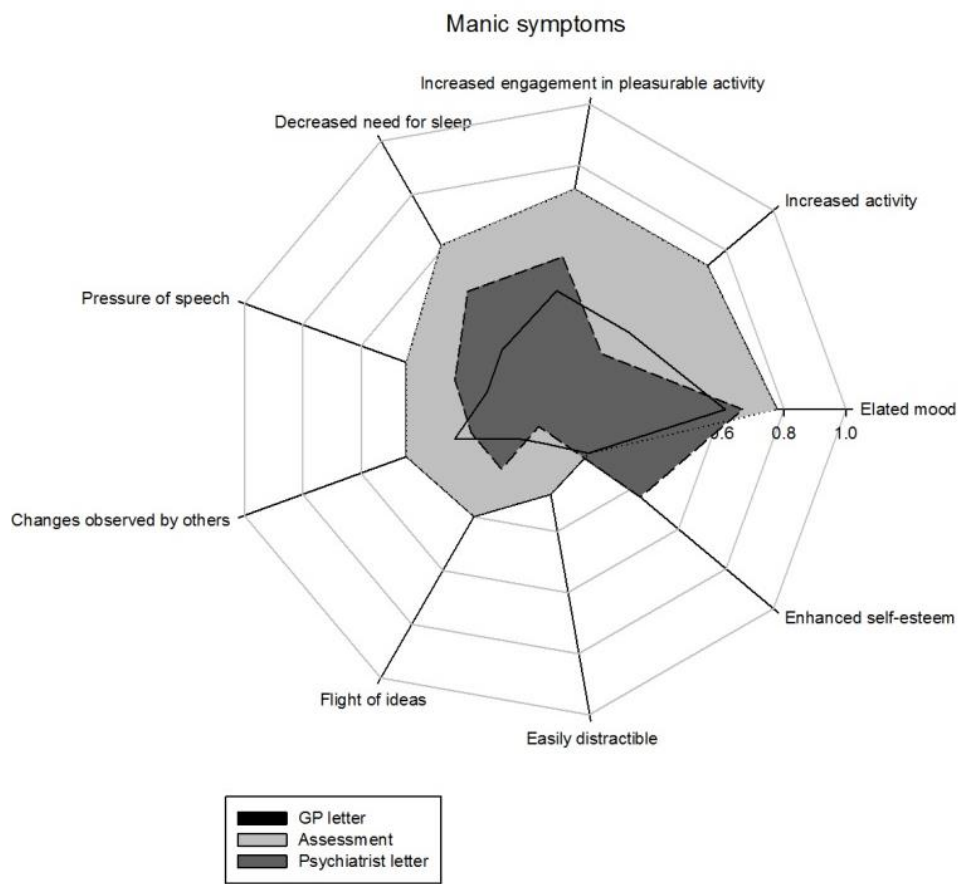


Fig 3.1.2 Proportion of diagnostic criteria for mania included in GP referral letters, assessment and psychiatrist letters.

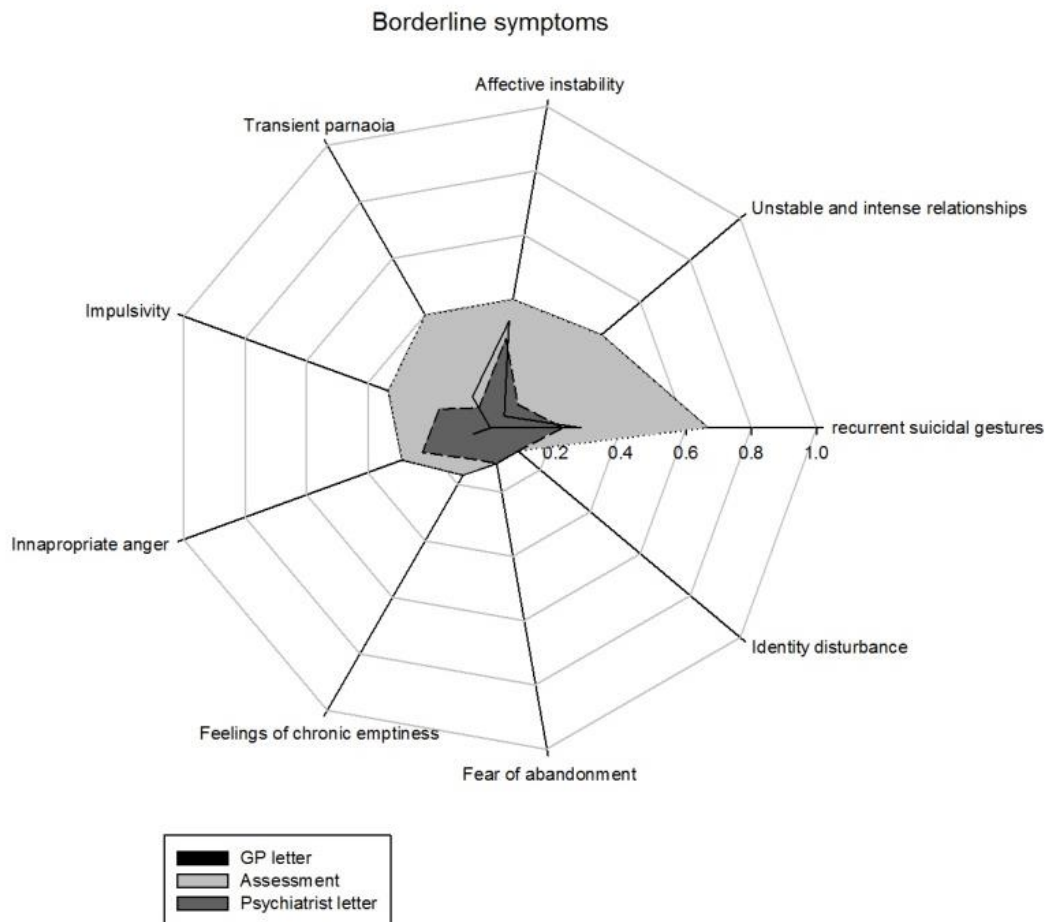


Fig 3.1.3 Proportion of diagnostic criteria for borderline personality disorder included in GP referral letters, assessment and psychiatrist letters.

Diagnoses

Letters to the general practitioner from the psychiatric team nevertheless contained diagnoses in 24/30 cases. Table 3.3 summarizes the symptom count towards different diagnoses recorded in the psychiatrist assessment and in the return letter to the GP. As might be expected, diagnoses were driven by symptoms positively identified in the assessment, but the absence of a systematic coverage of all the possible symptoms in the assessments is striking.

Diagnosis Given N (%)		Mean number of symptoms assessed (recording N=18)			Number of assessments where enough symptoms to make diagnosis were assessed (recording N=18)			Mean number of symptoms assessed (letter N=30)		
		Depression	Mania	Borderline personality disorder	Depression	Mania	Borderline personality disorder	Depression	Mania	Borderline personality disorder
Bipolar disorder	5	5.5	6.0	3.0	2	1	1	4.4	2.80	0.0
Borderline Personality disorder	4	3.0	3.5	5.5	1	0	1	3.4	2.6	2.8
Bipolar disorder & borderline personality disorder	1	N/A*	N/A*	N/A*	N/A*	N/A*	N/A*	4	7	5
Major depressive disorder	10	4.5	3.0	2.5	2	2	1	5.2	4.7	1.8
Cyclothymia	1	3.0	5.0	4.0	0	1	0	3.0	4.0	1.0
PTSD	1	N/A*	N/A*	N/A*	N/A*	N/A*	N/A*	6.0	6.0	2.0
No diagnosis given	6	5.5	4	1.5	3	1	0	3.67	3.0	0.83
No assessment letter written	2	7.0	7.0	4.0	2	2	1	N/A	N/A	N/A

*this assessment was not recorded

Table 3.3. Diagnoses given and symptoms assessed by psychiatrists

The reliability of the diagnoses against OPCRIT criteria was poor (Table 3.4).

Thus, of the 7 patients given a diagnosis of bipolar disorder or cyclothymia by their psychiatrist, only 3 had bipolar disorder when ICD-10 criteria were applied via OPCRIT; of the remaining 4, 1 had no diagnosis, 1 had major depressive disorder and 2 had a non-organic psychotic syndrome. Excluding the single diagnosis of borderline personality disorder, OPCRIT diagnoses accorded

exactly with the positive clinical diagnosis in only 5 cases out of 18. Additional diagnoses suggested by OPCRIT might have been clinically significant (e.g. 7 cases of possible alcohol misuse and or dependence) and in those given no diagnosis by a clinician 5 out of 6 had an axis 1 disorder when the OPCRIT checklist was applied (see table 3.4). ICD-10 criteria were employed as this was the mandated classification system within the electronic patient record locally. Differences in the diagnostic criteria for bipolar disorder and borderline personality disorder differ little between the two systems.

	Clinical diagnoses given following assessment						
ICD 10 diagnoses	Bipolar disorder	Borderline personality disorder	Major depressive disorder	Cyclothymia	PTSD	No diagnosis given	No assessment letter
Bipolar disorder*	3	1	0	0	0	1	0
Major depressive disorder	1	2	1	0		1	0
Non organic psychotic syndrome	1	2	3	1		1	2
PTSD	0	0	2	0	1	0	0
Agoraphobia	0	0	1	0	0	0	0
Social phobia	0	0	1	0	0	0	0
Harmful use of alcohol	0	0	0	0	1	1	0
Alcohol dependence	0	2	3	0	0	0	0
Harmful use of cannabis	0	0	1	0	0	1	0
Cannabis dependence	0	0	1	0	0	0	0
Substance misuse disorder	0	1	0	0	0	0	0
Other personality disorders	1	2	1	0	0	0	0
No diagnosis	1	0	2	0	0	1	0

*including manic episodes

Table 3.4. ICD-10 diagnoses generated by OPCRIT compared with diagnoses given following clinical assessment

OPCRIT does not generate DSM IV-TR or ICD-10 criteria for borderline personality disorder, so I was unable to assess the extent to which borderline personality disorder-specific information was objectively available for diagnosis. However, of the 5 patients given a diagnosis of borderline personality disorder

by the psychiatrist, the OPCRIT checklist suggested 1 had bipolar disorder, 2 had major depressive disorder, and 2 had a non-organic psychotic syndrome.

Discussion

This is the first study to explore the diagnostic process of clinicians attempting to distinguish bipolar disorder and borderline personality disorder. Referral letters from GPs contained some diagnostic information about depressive symptoms, although most were specifically querying the presence of bipolar disorder. The majority of diagnostic assessments these patients subsequently received were inadequate, as in only a small minority were symptoms of bipolar disorder or borderline personality disorder sufficiently assessed to establish the presence or absence of the diagnosis. The letters sent back to GPs did not fully detail the diagnostic criteria that were identified although the majority did attempt to give a diagnosis. These findings were at odds with how clinicians say they differentiate bipolar disorder and borderline personality disorder, which is by the use of the diagnostic criteria (see chapter 2). The OPCRIT procedure suggested that even in the presence of inadequate assessments (the OPCRIT output is wholly based on the information available to clinicians) clinicians regularly missed the presence of other comorbidities.

Identification of relevant symptoms

An ideal assessment or report would have extended over the maximum area possible, and all symptoms would have been included for all patients assessed.

The psychiatrist's letter added rather little to the GP letter in terms of symptom coverage. The actual assessments explored about twice the areas recorded in the letters, so are relevant, if not substantial, additions to the patient record. What is most striking is the poor coverage of manic and borderline symptom fields, where clinical assessments covered less than half the potential relevant items for diagnosis (see table 3.3).

There were few cases of exemplary practice. In only two assessments (both by junior CMHT clinicians) were enough symptoms explored for bipolar disorder and borderline personality disorder to be determined to be present or absent. Unstructured clinical assessment is the mainstay of psychiatric practice despite a wealth of evidence suggesting that, used in isolation, it is associated with inaccurate diagnoses (McGorry et al., 1995, Miller et al., 2001, van Praag, 1997). Thus, clinicians may simply fail to record symptoms they have in fact identified (Miller, 2002). Alternatively, they may use a top down approach to diagnosis focussing on the first cardinal symptom that comes to light, reaching a rapid diagnosis on the basis of this and then focussing on symptoms that are consistent with this diagnosis whilst dismissing those which are not and avoiding or ignoring other possible diagnoses (Elstein et al., 1978). My audio findings suggest that clinicians are simply failing to assess the relevant symptoms adequately at interview. Furthermore, the use of OPCRIT allowed me to demonstrate that poor reporting of certain symptoms is found across all clinical interactions with patients: significant numbers of symptoms were absent

even when I explored all available sources of information including patient records, letters and recordings.

Making a diagnosis

The failure to cover the relevant symptoms might be predicted to have had a relatively simple consequence: failure to make a diagnosis. In fact, diagnoses were offered in most cases. Diagnostic decisions were supported to some extent by symptom identification but they did not reflect a comprehensive assessment of all possible symptoms. Accordingly when such diagnoses were checked against OPCRIT criteria, only a minority were supported. Furthermore, the use of OPCRIT allowed us to demonstrate that poor reporting of certain symptoms is found across all clinical interactions with patients: significant numbers of symptoms were absent even when we explored all available sources of clinical information.

Discrepancies between clinical and research diagnoses have been described across a wide range of psychiatric conditions (Lewczyk et al., 2003) and a recent meta-analysis of studies comparing the two approaches found that the mean kappa for all psychiatric disorders was 0.27 (Rettew et al., 2009). For affective disorders (which included bipolar disorders) this dropped to 0.14. Oiesvold and colleagues (Oiesvold et al., 2012) explored the difference between clinician diagnoses recorded in case registers and those determined by an expert using a structured diagnostic system (the MINI plus) similar to OPCRIT. They found that, of 58 patients given a diagnosis of bipolar disorder

by an expert, only 17 (30%) had been given the diagnosis by a clinician, and the majority of these 17 patients had presented with mania as opposed to depression.

Limitations

I cannot determine whether the poor quality of assessments is specific to bipolar disorder and borderline personality disorder or true of psychiatric assessment more generally. While diagnosis is not always what GPs are seeking from psychiatrists, it was in the cases studied here. No firm conclusions can be drawn as to the true diagnosis as I did not conduct an independent diagnostic assessment of participating patients.

If there was a bias, it was probably to the inclusion of staff that were confident about their assessment skills because clinician participants self-selected into the study and identified which patient assessments should be included. The male gender bias in the clinician participants taking part was consistent with the gender split within the local trust. The audio recording of assessments might be expected to have positively enhanced practice.

Finally, the diagnostic output from OPCRIT was limited by the absence of much of the information required to specify diagnoses, and hence the large number of diagnoses of psychosis not otherwise specified.

The patient perspective

The present study was conducted in parallel with a qualitative study of the patient experience of assessment (Bilderbeck et al., 2014). Clearly patients value aspects of the assessment unrelated to the assessment of symptoms. These include sympathetic listening and being able to tell their story. However, they also described the clinicians' focus as being often on past events – implying a search for meaning in the patient's experience. It was interesting that patients themselves expressed the view that this focus seemed to neglect current problems actually related to symptoms. Finally, patients with unstable mood often valued a diagnosis (be it of bipolar disorder or borderline personality disorder). It is, therefore, notable that clinicians may be striving to make assessments more agreeable to patients at the expense of a clear focus on current symptoms. While it is often just these symptoms that are problematic for patients and which would allow psychiatrists to deliver a consistent diagnosis.

The findings presented in this chapter suggest that there is considerable scope for improving diagnostic practice. Education alone seems unlikely to be effective given the accurate recall of the diagnostic criteria among clinicians (as outlined in chapter 2). The view that standardized interviews may yield false positives was voiced by clinicians interviewed in chapter 2 suggesting that the introduction of such approaches into clinical practice may be met with resistance. The use of standardized interviews does have its limitations. They do not account for the context in which symptoms arise and may fail to provide clinical clarification. In general they are lengthy and it has been hypothesised that standardized interviews may be affected by the respondents lack of

motivation to give honest and thoughtful responses as well as by interview questions that exceed respondents' memory (Wittchen et al., 1999).

Others have suggested that semi-structured interviews, which would allow clinical judgement to be exercised whilst maintaining the coverage of a standardized diagnostic interview, might be appropriate for use in clinical practice (Brugha et al., 1999). However, similar mean kappas have been reported for structured versus semi-structured approaches (Rettew et al., 2009).

The widespread availability of new technologies and the move towards patient-accessible and patient-annotated health care records may have significant implications for diagnostic practice. As a more nuanced understanding of the objective markers of disease emerges (e.g. the changes in activity associated with mood (Faurholt-Jepsen et al., 2013)) a diagnostic system based solely upon clinical observations will become increasingly defunct. While such technologies are still in the early stages of development they are already a useful adjunct to clinical practice.

4. HOW CAN BIPOLAR DISORDER AND BORDERLINE PERSONALITY DISORDER BE DISTINGUISHED OBJECTIVELY? COHORT CHARACTERISTICS.

The overlapping diagnostic criteria of bipolar disorder and borderline personality disorder, namely mood instability and impulsivity, present clinicians with a challenge even were they to employ optimal diagnostic assessments. The reliance on retrospective self-report of mood states makes this particularly difficult not least because recall of mood states is inherently inaccurate and is influenced by the personal relevance of a given situation, recency and current affective state (Gray and Watson, 2007). In chapters 4-7 I describe a series of studies using cognitive tasks designed to distinguish bipolar disorder, borderline personality disorder and healthy volunteers. In this chapter, I will describe the recruitment strategy and clinical characteristics of the three groups. Only female participants were included because borderline personality disorder is more prevalent in women in clinical samples (Torgersen et al., 2001, Schwartz et al., 1990) and there are significant gender differences in its comorbidity and associated personality traits, with men having higher rates of substance misuse, more explosive temperaments and higher novelty seeking when compared to women (Sansone and Sansone, 2011, Banzhaf et al., 2012) .

Method

The study funded by the Oxfordshire Health Services Research Committee and was approved by the Oxfordshire NHS research ethics committee (OxRecA 10/H0604/64). All participants gave written informed consent.

Samples

Participants were female and aged between 18 and 60 years, 20 had diagnoses of DSM-IV borderline personality disorder, 20 of DSM-IV bipolar disorder (but without comorbid borderline personality disorder) and 20 were healthy volunteers with no history of psychiatric illness. Patients were recruited from community settings via posters, the department website, and CMHT clinicians. None of the participants had required hospital admission or crisis team support in the preceding month.

Power Calculation

On the basis of previous studies, involving individuals with borderline personality disorder and involving patients with bipolar disorder and, on the basis of other experiments using an iterated Prisoner's Dilemma (the task described in chapter 5), I estimated an effect size of 0.55. With 3 groups of subjects, group sizes of 20 in each provide a calculated power of 0.96 to detect a significant F-ratio of 3.17 at an error probability of 0.05.

Clinical assessment and psychometric measures***Diagnosis***

Participants were screened using the SCID-1 (Spitzer et al., 1992, Williams et al., 1992) and the borderline items from the International Personality Disorders Examination (IPDE) (Loranger et al., 1996) to confirm eligibility. The IPDE is a

semi structured clinical interview designed to assess the personality disorders in ICD-10 and DSM IV. It generates categorical diagnoses and dimensional scores based up on those categories. Inter-rater reliability and temporal stability for the borderline items have κ values of .80 and .70 respectively.

Mood

Depressive symptoms were measured using the Hamilton depression rating scale (HAM-D) (Hamilton, 1960). This is a 21-item clinician-rated scale which rates the severity of depression. It is widely used in clinical practice and pharmaceutical trials. All participants had a HAM-D score of less than 7 (deemed to be in the normal range). Manic symptoms severity was measured using the Young Mania Rating Scale (Young et al., 1978). This is an 11-item scale designed to be delivered by a clinician or trained rater. All participants had a score of less than 7.

Cognitive ability

Cognitive ability was estimated using Raven's Matrices (Raven et al., 2004). This is a measure of abstract reasoning included to control for the possible effects of cognitive ability on performance in experimental tasks.

Trait measures

Barratt Impulsiveness Scale (BIS-11)(Barratt, 1965): The BIS is a widely used self-report measure of trait impulsivity. It has three subscales: Motor impulsiveness, attention and non-planning impulsiveness.

Buss-Perry Aggression Questionnaire (AQ) (Buss and Perry, 1992): The AQ is a measure of trait aggression and has four subscales each addressing a different aspect of aggression: physical, verbal, anger and hostility.

Positive and Negative Affect Schedule (PANAS; (Watson et al., 1988)): This is a well validated 20-item self-report measure which rates average level of positive and negative affect.

Statistics

Differences between the participant groups in age and psychometric scores were analysed in SPSS version 20.0 (IBM Corp., 2011) by one-way analysis of variance (ANOVA) with the single factor of participant group. All post-hoc tests were completed using Tukey's honest significant difference (Tukey's HSD).

Results***Diagnoses***

Lifetime axis-1 disorders differed significantly across the three groups ($\chi^2(2)=60.0, p<0.001$) but were broadly similar across the two clinical groups (Table 4.1) with the exception of eating disorders which were more common in borderline personality disorder participants than bipolar disorder participants

($\chi^2(1)=3.58$, $p=0.058$). Mean dimensional scores on the IPDE differed significantly between groups ($F(2,57)=153.9$, $p<0.001$). Tukey's HSD indicated that borderline personality disorder was associated with significantly higher mean scores than bipolar disorder participants (mean $\pm$ SEM = 14.15 ± 0.87 vs 1.95 ± 0.51 , $p<0.05$), and healthy control participants (mean $\pm$ SEM = 14.15 ± 0.87 vs 0.55 ± 0.27 , $p<0.05$). Bipolar disorder was associated with higher mean scores than healthy control participants (1.95 ± 0.51 vs 0.55 ± 0.27 , $p<0.05$) however, no bipolar disorder or healthy control participant met criteria for borderline personality disorder.

Lifetime diagnosis	Borderline (N=20)	Bipolar (N=20)	Healthy control (N=20)	
Major depressive disorder	18	18	0	$\chi^2(1)=0.00$, $p=1.00$
Bipolar affective disorder	0	20	0	$\chi^2(1)=19.26$, $p<0.001$
Anxiety disorder	8	4	0	$\chi^2(1)=1.91$, $p=0.17$
OCD	3	3	0	$\chi^2(1)=0.00$, $p=1.00$
PTSD	3	1	0	$\chi^2(1)=1.11$, $p=0.292$
Psychotic disorder	4	1	0	$\chi^2(1)=2.06$, $p=0.151$
Eating disorder	7	2	0	$\chi^2(1)=3.58$, $p=0.058$

Table 4.1 Lifetime axis-1 diagnoses for 20 individuals with DSM-IV borderline personality disorder, 20 (euthymic) individuals with DSM-IV bipolar disorder and 20 healthy controls (significance shown for clinical group comparisons only).

Suicidal behaviour

Significant differences in suicidal behaviour ($\chi^2(2)=33.60$, $p<0.001$) and non-suicidal self-injury ($\chi^2(2)=28.1$, $p<0.001$) were observed between groups

Participants with borderline personality disorder were significantly more likely to have engaged in suicidal behaviour compared to bipolar disorder participants ($\chi^2(1)=4.8$, $p=0.028$). Non suicidal self-injury was also more common among borderline personality disorder participants when compared to those with bipolar disorder ($\chi^2(1)=10.1$, $p=0.001$). No suicidal behaviour or non-suicidal self-injury was observed in the healthy control group.

Psychometrics

The borderline personality disorder, bipolar disorder and control participants were matched for age ($F(2,57)=0.524$, $p=0.595$) and cognitive ability as measured by the Raven's Matrices ($F(2,57)=1.174$, $p=0.316$) (Table 4.2).

Current symptoms of depression and mood elevation were low, although HAM-D scores differed significantly between groups ($F(2,57)=13.5$, $p<0.001$).

Tukey's HSD indicated that the borderline personality disorder group had significantly higher scores on the HAM-D compared to the bipolar disorder group ($p<0.05$) and controls ($p<0.05$) (Table 4.2). Significant differences in trait and state positive affect ($F(2,57)=4.391$, $p=0.017$ and $F(2,57)=4.539$, $p=0.014$) and trait and state negative affect ($F(2,57)=26.9$, $p<0.001$ and $F=12.16$, $p<0.001$) were observed between the three groups. Tukey's HSD indicated that participants with borderline personality disorder reported higher state and trait

negative affect ($p < 0.05$) than bipolar participants and healthy controls and lower state and trait positive affect ($p < 0.05$) compared to healthy controls. Bipolar participants reported greater trait negativity ($p < 0.05$) compared to healthy controls.

Impulsivity (BIS-11) differed significantly between groups ($F(2,57) = 13.275$, $p < 0.001$). Tukey's HSD indicated that borderline personality disorder was also associated with significantly higher impulsivity compared to bipolar disorder ($p < 0.05$) and controls ($p < 0.05$). Bipolar participants had significantly higher trait impulsivity than healthy controls ($p < 0.05$).

Self-reported aggression (AQ) differed significantly between the three groups ($F(2,57) = 19.62$, $p < 0.001$). Tukey's HSD indicated that borderline participants reported higher levels of aggression than bipolar participants ($p < 0.05$) and healthy controls ($p < 0.05$). While total aggression scores did not differ between bipolar participants and healthy controls ($p > 0.05$), bipolar participants reported significantly higher hostility ($p < 0.05$).

Mean (SE)	Borderline (N=20)	Bipolar (N=20)	Healthy controls (N=20)	ANOVA
Age	33.65 (2.56)	36.1 (2.37)	32.7 (2.24)	ns
Ravens matrices	47.53 (1.42)	50.95 (1.53)	50.15 (1.9)	ns
HAM-D	3.85 (0.44)	2.40 (0.49)	0.80 (0.28)	p<0.001
YMRS	0.55 (.24)	0.30 (0.147)	0.10 (0.07)	ns
BIS	74.7 (2.83)	67.85 (3.20)	55.4 (1.82)	p<0.001
BUSS-PERRY	85.45 (3.45)	61.05 (3.80)	53.7 (3.98)	p<0.001
Physical	22.60 (1.97)	13.95 (1.09)	14.05 (1.74)	p<0.001
Verbal	13.70 (0.84)	11.65 (1.61)	12.20 (0.88)	ns
Anger	21.05 (1.43)	15.50 (1.23)	13.75 (1.47)	p=0.001
Hostility	26.65 (1.24)	18.30 (1.84)	12.90 (1.00)	p<0.001

Table 4.2 Comparison of self-rating of demographics and self-reported trait and state affect, aggression and impulsivity in 20 individuals with DSM-IV borderline personality disorder, 20 (euthymic) individuals with DSM-IV bipolar disorder and 20 healthy controls.

Treatment

Pairwise comparisons revealed that borderline personality disorder participants were significantly more likely to be taking antidepressant medication ($\chi^2(1)=3.600$, $p=0.058$) or receiving psychological treatment ($\chi^2(1)=6.144$, $p=0.038$) than the bipolar disorder participants and the healthy controls (Table 4.3). However, there was no significant overall difference between the number of participants from each of the two clinical groups taking psychotropic medication ($\chi^2(1)=2.133$, $p=0.144$).

	Borderline (N=20)	Bipolar (N=20)	Healthy controls (N=20)	Pairwise comparisons of borderline and bipolar groups.
Any psychiatric med.	13 (65%)	17 (85%)	0 (0%)	$\chi^2(1)=2.133$, $p=0.144$
Antidepressant	13	7	0	$\chi^2(1)=3.600$, $p=0.058$
Antipsychotic	8	12	0	$\chi^2(1)=1.600$, $p=0.206$
Mood stabiliser	4	8	0	$\chi^2(1)=1.905$, $p=0.168$
Lithium	1	5	0	$\chi^2(1)=3.137$, $p=0.077$
Benzodiazepines	4	2	0	$\chi^2(1)=0.784$, $p=0.376$
Hypnotics	2	0	0	$\chi^2(1)=2.147$, $p=0.147$
Current psychological treatment	9	3	0	$\chi^2(1)=6.144$, $p=0.038$

Table 4.3 Current treatment of 20 individuals with DSM-IV borderline personality disorder, 20 (euthymic) individuals with DSM-IV bipolar disorder and 20 healthy controls (significance shown for clinical group comparisons only).

Seventy percent (14/20) of the borderline personality disorder group and 50% (10/20) of the bipolar disorder group had been admitted to psychiatric hospitals in the past. Of these 28.6% (4/14) of the borderline personality disorder group and 60% (6/10) of the bipolar disorder group had been detained under the Mental Health Act.

Marital and employment status

No significant differences in marital status were found between the three groups (single status was reported by 11 vs 11 vs 6 for borderline personality disorder, bipolar disorder and HC respectively, $\chi^2(2)=3.348$, $p=0.187$) and there were no significant differences between the groups with respect to having children (3 vs

5 vs 6 for borderline personality disorder, bipolar disorder and healthy controls respectively, $\chi^2(2) = 1.304$, $p = 0.521$). Significant differences in employment status were observed between groups (3 vs 11 vs 10, $\chi^2(2) = 7.917$, $p = 0.019$ for borderline, bipolar and healthy participants respectively). Borderline personality disorder participants were significantly less likely to be employed compared with bipolar disorder participants ($\chi^2(1) = 7.03$, $p = 0.008$) and healthy controls ($\chi^2(1) = 5.584$, $p = 0.018$) however there was no significant difference in employment status between the bipolar disorder and healthy control participants ($\chi^2(1) = 0.382$, $p = 0.537$).

Fourteen participants in the borderline personality disorder group and nine in the bipolar disorder group reported early physical or sexual abuse compared with none in the healthy control group. There was no significant difference between the two clinical groups ($\chi^2(1) = 2.56$, $p = 0.11$).

Discussion

The matching of age, IQ and current symptoms between the three experimental groups is important as it means that any behavioural differences identified in the cognitive tasks are much less likely to be explained by differences in these three domains. The three groups were matched for age, IQ and current symptoms although self-reported mood symptoms differed significantly between groups. Comorbidity was largely similar between the two clinical groups as was overall treatment although current psychological treatment and antidepressants were more common among borderline personality disorder participants. The psychometric characteristics of the three groups differed with respect to

aggression and impulsivity, but pairwise comparisons suggested there were few differences between the two clinical groups.

Discrepancies between self-report and behavioural measures in borderline personality disorder have been previously described (Jacob et al., 2010). Self-report measures of affective state may be problematic in borderline personality disorder because of the confounding effects of impaired emotional awareness and deliberate attempts to avoid experiencing aversive internal states and a dramatic presentation style (Levine et al., 1997). It seems likely that it is this confound that explains the differences between the self-reported mood symptoms and those derived from clinician interview.

The prominence of antidepressant (largely selective serotonin reuptake inhibitors) prescribing in the borderline personality disorder group is consistent with national surveys (POMH-UK, 2012) and other studies of borderline personality disorder (Rentrop et al., 2008, Schuermann et al., 2011, Crawford et al., 2011). The significant differences in antidepressant prescribing between the borderline personality disorder and bipolar disorder groups may reflect recent changes in the guidance. Antidepressants lack superior efficacy when compared to mood stabilisers alone when used in the treatment of bipolar disorder. (Goodwin and Consensus Group of the British Association for Psychopharmacology, 2009). No antidepressant has a specific license for use in borderline personality disorder (National Collaborating Centre for Mental Health, 2009), but they continue to be commonly prescribed in an attempt to

improve mood symptoms. Similarly, the higher rates of current psychological treatment in borderline personality disorder are consistent with current treatment guidelines (National Collaborating Centre for Mental Health, 2009) and may also reflect the availability of a personality disorder-specific service in the local area.

Medications may impact performance in the cognitive tasks. Antipsychotics (de Bruijn et al., 2006b), antidepressants (Wadsworth et al., 2005), mood stabilisers (Meador et al., 1995) and lithium (Stip et al., 2000) have all been found to impair performance in healthy control groups. In clinical groups the impact is more complex as treatment of the underlying illness with antipsychotics for example, may enhance cognitive performance (Macqueen and Young, 2003, Dias et al., 2012). Both clinical groups are matched overall for psychotropic medication and the potential for the excess of SSRI prescribing in the borderline group to influence the between group differences in each cognitive task is discussed in more detail in the subsequent chapters.

The employment status of the three groups differed significantly. The significantly lower employment status of those with borderline personality disorder is consistent with that reported in other studies (Gunderson et al., 2011a). The poor employment status is likely to reflect the pervasive nature of borderline personality disorder and its impact on educational attainment and social function. By contrast bipolar disorder is more episodic in nature as thus less likely to pose such a barrier to employment.

The characteristics of the three participant groups is similar to those described in the literature. Unlike many similar studies (particularly those in borderline personality disorder) participants are derived from a community rather than inpatient environment, and are likely to be representative of those patients where the diagnostic uncertainty most commonly arises.

5. SOCIAL BEHAVIOUR IN BIPOLAR DISORDER COMPARED TO BORDERLINE PERSONALITY DISORDER

In this experiment, I investigated the hypothesis that borderline personality disorder and bipolar disorder can exhibit divergent behaviours in the context of social exchanges. Mood instability in borderline personality disorder is most powerfully expressed in the context of disrupted interpersonal relationships. Such interpersonal difficulties have been linked to impairments in decoding social signals, such as facial expression (Minzenberg et al., 2006), or deeper problems in trusting the motives and actions of others (Lieb et al., 2004, Fonagy and Bateman, 2006). By contrast, mood instability in bipolar disorder is traditionally seen as primary, and not attributed to comparable social impairments because social and occupational function can be high (Kusznir et al., 2000). I hypothesised that difficulties with cooperative behaviour in a laboratory setting would be more marked in individuals with borderline personality disorder than individuals with bipolar disorder and controls. This would occur despite the common breakdown of relationships and professional position in bipolar disorder, and problems with affective decision making (Adida et al., 2011), emotion recognition and theory of mind (Martino et al., 2011). In other words, disrupted social exchanges may be a primary locus of psychopathology in borderline personality disorder.

Game theory offers numerous models that can be used to characterise how interactions with other people can depart from what is rational and most advantageous (Webb, 2006). This has the potential to illuminate clinical

psychopathology (Sharp et al., 2012). Borderline personality disorder patients appear to lack the capacity to sustain mutually beneficial interactions with playing partners in an investment-trust game (King-Casas et al., 2008).

Decision-making in this context was associated with diminished insula activation in response to investment when compared to healthy controls. Here I tested, for the first time, the way that borderline personality disorder patients and bipolar disorder patients cooperated with social partners in a cooperative decision-making context. I used an iterated (simultaneous) Prisoner's Dilemma (PD) game. PD games are now the classic mixed-motive formulation of the simple human dilemma in which 2 players must make choices to 'cooperate' or 'defect' for their sole or joint benefit. In their iterated form, PD games can provide an estimate of how individuals acquire and maintain patterns of reciprocal altruistic behaviour (Axelrod and Hamilton, 1981). Cooperation can produce better outcomes for both parties, but risks exploitation by partners; defection can maximise immediate benefits, but at the risk of the breakdown of mutually beneficial exchanges.

There were three important elements in the design of the study. First, I implemented PD games in which the participant's playing partner adopted a tit-for-tat strategy, repeating the last choice of the participant automatically.

Extensive research shows that tit-for-tat is an effective strategy for eliciting cooperation from social partners (Axelrod and Dion, 1988) and therefore for measuring putative deficits in borderline personality disorder or bipolar disorder.

Second, I included only female participants because in borderline personality disorder there are significant gender differences in its comorbidity (Tadic et al.,

2009) and associated personality traits including novelty seeking (Sansone and Sansone, 2011). Finally, to be sure that any sub-optimal behaviour in the PD game was not due to problems with basic processing of social stimuli, I included a choice-reaction time task to test the ability to use joint attention to speed categorisation of visual targets. This latter task also provided an appropriate control for motivational deficits in the two clinical samples.

Method

The study was funded by the Oxfordshire Health Services Research Committee and approved by the Oxfordshire NHS research ethics committee (OxRecA – 10/H0604/64). All participants gave written informed consent.

Participants

The participant groups are described in chapter 4.

The iterated Prisoners Dilemma (PD) game

Before playing the game, participants were introduced to a female 'playing partner'. In reality, this was a member of staff or student volunteer who acted as a confederate. It was explained that her computer was networked from another room in the building where she would be situated. In fact, the playing partner's choices were entirely automated and generated by the computer programme in a pre-programmed fashion (see below).

I used an iterated (simultaneous) PD game previously similar to that reported by Rilling et al (2002). On each round of the PD game, participants were shown a visual display showing a 2x2 pay-off matrix (Figure 5.1) which defined the 4 possible outcomes of each round (or trial) of the game: both players could cooperate (CC); participants could cooperate while their partners defected (CD), participants could defect while the partners cooperated (DC), or both players could defect (DD). The payoffs for these outcomes conformed to the rule: $CD > CC > DD > DC$, and $CC > (CD + DC)/2$. Participants were asked to cooperate or defect by pressing C or D on a standard keyboard. Both players (in this case the participant and the computer) made their choices simultaneously; i.e. without knowledge of their partner's choice to cooperate or defect. Choices are then revealed simultaneously. If a PD game is played just once, the rational choice for any participant is to defect. This way she will do at least as well as her partner regardless of their own choices. However, in an iterated game, the rational strategy is to seek mutual cooperation, which maximizes the gains of both players.

Round 1

Choose to Co-operate or Defect

	CO-OP	DEFECT
CO-OP	40p (40p)	70p (0p)
DEFECT	0p (70p)	20p (20p)

Figure 5.1. Payoff matrix for the four outcomes of an iterated, simultaneous Prisoner's Dilemma (PD) game played by 20 individuals with DSM-IV borderline personality disorder, 20 (euthymic) individuals with DSM-IV bipolar disorder and 20 non-clinical healthy controls. (All 3 groups were matched for age and cognitive ability.) Participants' options are listed atop columns and partners' choices (in fact, a computer program playing tit-for-tat) are listed aside the rows. The payoffs for each player, depending upon both players' choices, are shown within each square; green= participants and red= partners).

Participants played 2 PD games, each consisting of 20 rounds. The 'partner' started the first game by cooperating, and the second game, by defecting; thus, instantiating both cooperative and non-cooperative behaviour. Before starting, participants played 4 training rounds that demonstrated the 4 possible outcomes (CC, CD, DC and DD). At the end of the experimental session, participants were debriefed about the deception and specific consent was sought to use their data. All participants had believed they were playing with a real human partner.

Predictive Gaze Cueing

Twenty faces from the NimStim face database (Tottenham et al., 2009) were arranged in pairs matched for gender, ethnicity and approximate age (Bayliss et al., 2009). All faces held a moderately positive (smiling) expression and were initially presented looking straight ahead. One of each pair was designated to Face Group A or to Face Group B. Each group comprised 2 pairs each of black males and black females, and 3 pairs of white males and white females.

Previously, twelve independent raters had ensured that the pairs of faces were rated equal attractiveness and trustworthiness, and that, as a whole, Face Groups A and B were of roughly equal attractiveness and trustworthiness (Bayliss et al., 2009). The target to-be-categorised stimuli comprised pictures of 36 household objects, 18 of which were categorised as belonging in the kitchen and 18 in the garage.

At the start of each trial, participants fixated a central cross on the computer display. Following an interval of 600ms, the cross was replaced by a face (see fig 5.2). After another 1500ms, the eyes of the face looked to the right or left. A household object appeared 500ms later on the left or right of the display.

Participants were instructed to decide, quickly and accurately, whether the object belonged in the garage ('h' key) or kitchen (spacebar key). If no response was made after 2500ms, the trial was coded as an error, and the next trial presented. A blank screen was displayed for a 1500ms inter-trial interval.

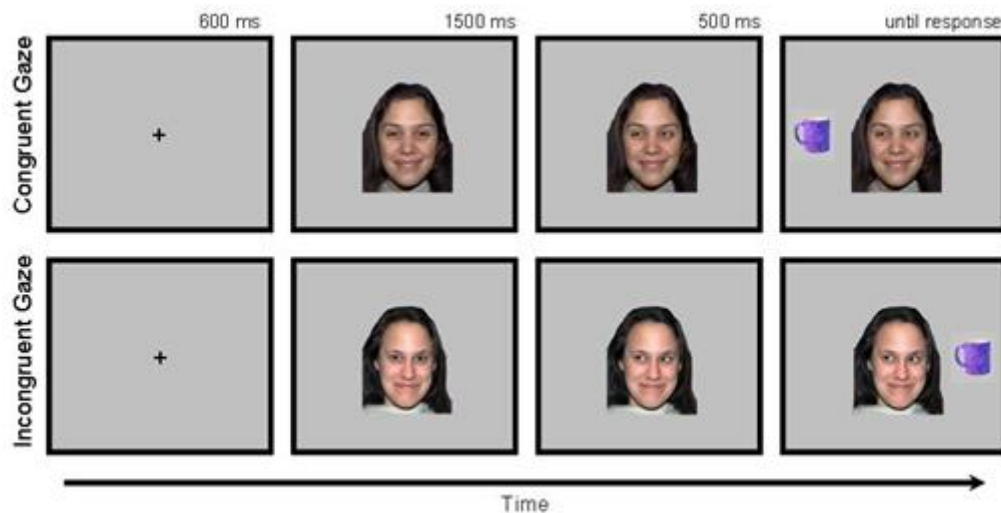


Figure 5.2 Trial structure for the gaze-cueing task, showing the presentation of a fixation cross, followed by a face, a shift in fixation to the left or the right and, finally, a target object for categorisation. Valid faces were followed by objects presented on the same side as the shifted fixation; invalid faces were followed by objects on the opposite side.

Participants completed 2 blocks of 120 trials, with 10 'valid' faces that always looked towards the location of the subsequent target object and 10 'invalid' faces that always looked in the opposite location (appearing 12 times in a random order, with randomly selected targets).

Statistics

Prisoner's Dilemma. The proportion of cooperative responses was arcsine transformed for statistical analysis (as is appropriate whenever variance is proportional to the mean (Howell, 1987)). The proportion of cooperative responses and mean deliberation times were analysed with mixed ANOVAs with the between-subject factors of group and the within subject factor of game (1st or 2nd). The proportion of cooperative choices following each of the 4 game

outcomes (mutual cooperation (CC), defection with partner cooperation (DC), cooperation with partner defection (CD) and mutual defection (DD)) were analysed with mixed ANOVAS with the between-subject factor of group and the within-subject factor of immediately previous outcome. All post-hoc tests were completed using one-sample T-tests or Tukey's HSD. Tables, figures and text report the original untransformed data.

Predictive gaze-cueing. Reaction times (ms) and the proportion of incorrect responses were analysed using mixed ANOVAs with the between-subject factors of group and the within-subject factor of cue validity. Trials with reaction times greater than 1500ms were excluded as per the methodology employed by Rogers et al (2014).

Results

The clinical characteristics of the three groups are described in chapter 4.

Iterated Prisoner's Dilemma Game

Borderline personality disorder participants made significantly fewer cooperative responses while playing the 2 iterated PD games compared with the bipolar disorder and healthy control participants (see Figure 5.3; $F(2,57)= 4.243$). Post-hoc Tukey tests showed that the borderline personality disorder participants cooperated less frequently (0.5072 ± 0.0327) than both of the bipolar disorder participants (0.698 ± 0.059) and controls (0.679 ± 0.056), $p < 0.05$. By contrast, a

post-hoc Tukey test revealed there was no difference in the proportion of cooperative responses in bipolar disorder participants compared to the controls ($p=0.964$).

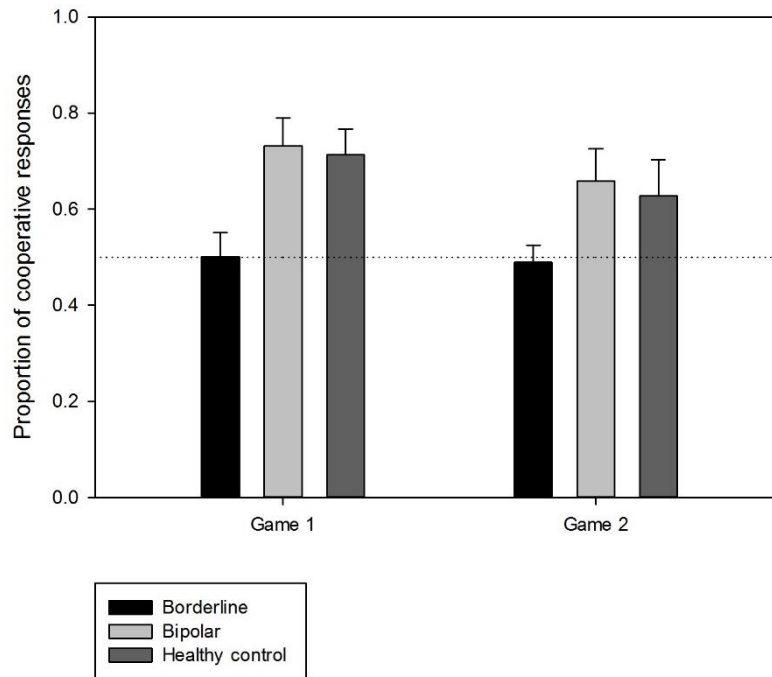


Figure 5.3 Mean proportion of cooperative choices of 20 individuals with DSM-IV borderline personality disorder, 20 (euthymic) individuals with DSM-IV bipolar disorder and 20 non-clinical healthy controls in 2 iterated Prisoner's Dilemma games. In Game 1, playing partners opened with cooperative choices and then played (strict) tit-for-tat; in Game 2, playing partners opened with a defection and then (strict) played tit-for-tat. The dashed horizontal line indicates chance levels of cooperation rates (i.e. 0.5).

Both the bipolar disorder participants and healthy control participants tended to make fewer cooperative responses on the 2nd game compared to the 1st game (in response to their playing partners' opening defection). ($F(2,57)=1.90$, $p=0.175$). However, this effect was absent for borderline personality disorder participants, their cooperative responses did not markedly change between the 1st and the 2nd game (see Fig. 2; $(0.50\pm0.050$. vs. 0.51 ± 0.036 , $F(1,19)=0.13$).

One-sample t-tests against a baseline of 0.5 confirmed that both the bipolar disorder participants and HCs tended to cooperate more frequently than they defected across the 2 games, $t(19)= 3.331$, $p=0.004$ and $t(19)= 3.178$, $p=0.005$). By contrast, the proportions of cooperative responses in the borderline personality disorder were no greater than chance, $t(19)= 0.219$, $p= 0.829$.

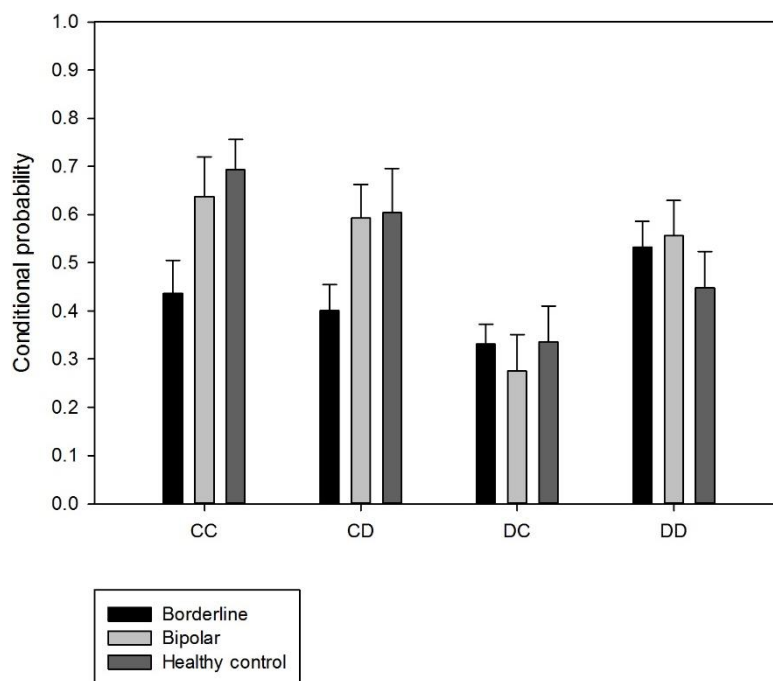


Figure 5.4. The proportion of cooperative choices following each of the 4 possible outcomes of the previous round of an iterated Prisoner's Dilemma games in 20 individuals with DSM-IV borderline personality disorder, 20 (euthymic) individuals with DSM-IV bipolar disorder and 20 non-clinical healthy controls (CC= both players cooperated (mutual cooperation); CD= participants cooperated while partners defected; DC= participants defected while partners cooperated; or both players could defect (mutual defection, DD)).

All participants were faster to make their choices in the 2nd PD game than the 1st game ($F(1,57)=37.86$, $p<0.001$) (see Table 5.1). Participants were also slightly (and non-significantly) faster to cooperate than defect ($F(1,57)=2.432$,

$p=0.125$). There were no significant differences between the 3 groups in the times needed to decide to cooperate ($F(2,57)=0.521$) or defect ($F<1$). The borderline personality disorder participants finished the PD games with smaller winnings compared to the bipolar disorder participants and the controls (£12.52 vs £13.65 and £13.72 respectively) where, consistent cooperative behaviour would have yielded maximal winnings of £15.60. However, this reduction in winnings was not quite significant, $F(2,57)=2.33$, $p=0.11$.

	Deliberation time in milliseconds (SE)	
	Game 1	Game 2
Bipolar	1943.43 (244.2)	1447.84 (226.29)
Borderline	1894.98 (160.38)	1324.76 (181.12)
Healthy controls	1766.25 (183.94)	1162.59 (112.60)

Table 5.1. Mean deliberation times (ms) for decisions to cooperate or defect across 2 iterated Prisoner's Dilemma games in 20 individuals with DSM-IV borderline personality disorder, 20 individuals with DSM-IV bipolar disorder and 20 healthy controls.

Finally, there were no significant associations between the proportions of cooperative responses on the one hand and trait scores of either impulsivity (BIS-11) or aggression (AQ) on the other hand within either the borderline personality disorder or the bipolar disorder group, all $r_s < .150$. No significant differences in the proportion of cooperative responses was found to be associated with early abusive experiences in the two clinical groups (0.62 ± 0.061 vs 0.59 ± 0.046 , $F(1,38)=0.172$, $p=0.681$).

Predictive gaze-cueing

Overall, mean reaction times when categorising target objects as belonging in 'garage' vs 'kitchen' did not significantly differ between groups ($F(2,57)= 0.623$, $p= 0.540$) (see Figure 5.5). Mean reaction times ($\pm$ SEM) were significantly faster following presentation of valid compared to invalid faces (779.64 ± 13.02 vs. 814 ± 13.59 ms, respectively). However, there was no evidence that this facilitation was markedly altered in the borderline personality disorder participants (802.91 ± 24.6 vs. $831.67\text{ms}\pm24.15$), bipolar disorder participants (773.55 ± 23.63 vs $809.51\text{ms}\pm27.98$) and healthy controls (762.14 ± 19.339 vs. $803.30\text{ms}\pm18.76$) ($F(2,57)=0.623$, $p=0.540$).

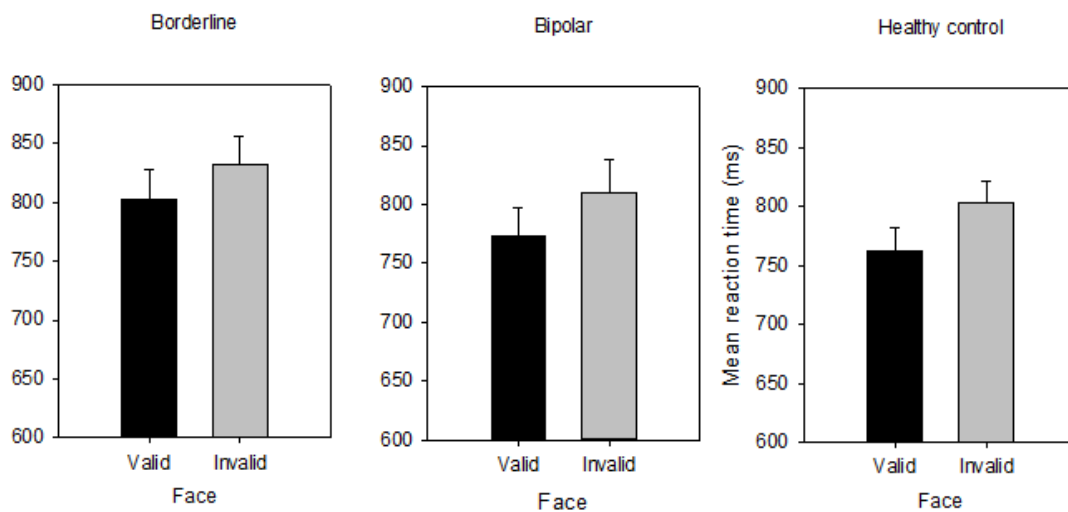


Figure 5.5. Mean correct reaction time (ms) for object-categorisations following the presentation of spatially-predictive gaze-cues (in 'valid' vs. and 'invalid' faces) in 20 females with diagnoses of DSM-IV borderline personality disorder, 20 females with DSM-IV bipolar-1 disorder and 20 age- and cognitive ability-matched control participants.

Mean error rates were less than 6%, and there were no differences in the proportion of errors that were observed between the three groups (0.054 ± 0.013

vs 0.040 ± 0.006 vs 0.044 ± 0.008 for bipolar disorder, borderline personality disorder and healthy controls respectively $F(2,57)=0.474$, $p=0.627$). Overall, participants made marginally fewer errors following the presentation of valid compared to invalid faces ($4.42 \pm 0.54\%$ vs. $5.00 \pm 0.508\%$; $F(1,57)=1.783$, $p=0.187$).

Discussion

In this experiment, I found that females with diagnoses of DSM-IV borderline personality disorder showed patterns of reduced cooperation when compared to those with bipolar disorder and healthy control females in two iterated PD games. In its iterated form, the PD presents a classical dilemma between self-interest and reciprocal cooperative behaviour in which social partners can make small sacrifices for their joint benefit but at the risk of exploitation, thus exhibiting reciprocal altruism (Axelrod and Dion, 1988). In contrast to the other two groups, the borderline personality disorder participants failed to cooperate more frequently than chance and failed to sustain cooperation following previous cooperative exchanges with their playing partners. The groups were matched for age, cognitive ability and current symptoms with the bipolar disorder and control groups, who did develop the expected pattern of mutual cooperation with their partners. Therefore, these findings provide support for the hypothesis that borderline personality disorder is associated with difficulties in establishing and maintaining reciprocally cooperative relationships with a known and gender-matched social partner. By contrast, these deficits were absent in the bipolar disorder patients.

Before discussing the implications of these findings, I consider some methodological issues. First, both clinical groups were taking psychotropic medications, with an excess of antidepressant treatment in the borderline personality disorder group (see chapter 4). However, there was no indication of a non-specific effect of medication upon performance in the PD game or the gaze-cueing task. Fluoxetine has been linked to pro-social behaviour in naturalistic (Raleigh et al., 1991) and experimental settings (Knutson et al., 1998), so higher prescription might have been expected to enhance cooperation in the borderline personality disorder group (which did not occur). The same effect might be expected of psychological treatments, but only 5 of the borderline personality disorder participants had attended group psychotherapy (and only 2 had completed the programme). Current mood symptoms could have contributed to group differences but all participants had HAMD and YMRS scores of less than 7 so are unlikely to be clinically significant.

Second, these findings are unlikely to reflect non-specific cognitive difficulties in processing social signals. Borderline personality disorder participants shifted their visual attention on the basis of another person's direction of gaze just as effectively and quickly as the controls, and their deliberation times to cooperate or defect were not slowed in the PD games. These observations also argue against the possibility that the diminished cooperation shown by borderline personality disorder participants reflects a general lack of engagement, a more basic motivational deficit, or the effects of current medication. Finally, early

abusive experiences are often highlighted in borderline personality disorder as possibly shaping psychopathology (Zanarini et al., 1989). However, between the clinical groups, there was no significant difference in the number participants who reported early physical and/or sexual abuse (14 vs 9, $\chi^2(1)=2.56$, $p=0.110$). Moreover, the proportion of cooperative responses in those participants who reported early abuse was not significantly higher than in those who reported no abuse, again suggesting that reduced cooperation in the borderline personality disorder is not attributable simply to early abusive experiences.

Tit-for-tat promotes cooperation in an iterated PD game for three reasons. First, it rewards cooperation but punishes defection. Second, it is clear: cooperative responses [or defections] are rewarded [or punished] immediately in the following round of the game, helping players to link their own behaviour to the responses of their partners. Third, tit-for-tat is forgiving: players who have defected but then revert to cooperation are immediately rewarded with matching cooperative behaviour by their partners. Accordingly, the proportion ($\pm$ SEM) of cooperative responses in the controls was above chance in the first and second PD games (0.708 ± 0.054 ; 0.635 ± 0.076), consistent with previous findings (Wood et al., 2006, Rilling et al., 2002). However, the borderline personality disorder participants failed to show statistically significant cooperation in either game (0.503 ± 0.050 ; 0.510 ± 0.036).

The data also help to clarify the character and extent of social deficits in euthymic bipolar disorder. Previous reports suggest problems with emotion recognition, theory of mind and affective decision making (Martino et al., 2011, Adida et al., 2011). This might suggest that the capacity of the bipolar disorder participants to anticipate the probable responses of playing partners or make cooperative choices might also be degraded. However, the euthymic bipolar disorder patients were just as capable of developing cooperative relationships as healthy controls. This reflects clinical observations that stable bipolar disorder patients frequently sustain high levels of social and occupational function.

There are at least three mechanisms that might contribute to the failure of the borderline personality disorder participants to acquire and sustain cooperation. First, high trait aggression and hostility are clinically obvious features of borderline personality disorder and may have mediated the failure of the borderline personality disorder patients to cooperate in the PD game. Second, impulsivity in borderline personality disorder involves both decisional as well as motor processes (Svaldi et al., 2012, Lawrence et al., 2010) and it may be that the borderline personality disorder participants were unable to resist the temptation to maximise their immediate reward by defecting when their partners had cooperated. Both of the above possibilities are plausible. However, neither AQ hostility nor impulsivity scores were linked to the proportion of cooperative responses in any of participant groups, while the bipolar disorder participants were indistinguishable from the controls despite elevated scores on the BIS-11 and the hostility sub-scale of the AQ. Moreover, if aggression or hostility played

significant roles in the behaviour of the borderline personality disorder participants, levels of cooperation *below* chance rather than the (more or less) equal cooperation and defection should have been observed.

Third, reduced cooperation could reflect diminished reward value assigned to the experience of mutual cooperation by borderline personality disorder participants. Previously, mutually cooperative outcomes in the PD game in healthy volunteers elicited elevated BOLD signals within the ventral striatum (Rilling et al., 2002). Diminished reward value of mutual cooperation could be the corollary of failures to sustain relationships between individuals with borderline personality disorder and their social partners. Further support for this possibility is provided by the diminished probability of further cooperative responses following mutually cooperative exchanges in the borderline personality disorder participants compared to the bipolar disorder patients and the healthy controls. The findings suggest that the experience of joint cooperation may not be coded or experienced as rewarding for borderline personality disorder participants as it is for bipolar disorder and healthy controls, and consequently cannot then provide a basis for sustained future cooperation with even known social partners.

Inspection of the conditional probabilities provides a further clue about the difficulties with cooperative behaviour in borderline personality disorder. In the only other comparable experiment using an investment game, borderline personality disorder participants failed to increase the profits returned to less generous investors as a prompt to increase their next investment (King-Casas

et al., 2008). This was interpreted as an unwillingness or inability to use 'coaxing' behaviours to repair or improve stressed or vulnerable relationships. Here, outcomes in which participants cooperated but their partners defected (DC) often elicit further cooperation as attempts to coax partners into cooperating again. This behaviour was absent in the borderline personality disorder participants, in contrast to the 'repairing' behaviour shown by the bipolar disorder and healthy controls, again possibly indicating the diminished reward value of future cooperation in borderline personality disorder.

Overall, the findings do not support suggestions that borderline personality disorder can be simply understood as a mood dysregulation disorder, allied with the bipolar spectrum. These results demonstrate for the first time that individuals with borderline personality disorder, but not individuals with bipolar disorder, fail to form reciprocally cooperative relationships with social partners in an iterated PD game. This behaviour may be mediated by or associated with a failure to derive reward value from mutual cooperation in social exchanges. I propose that this deficit underlies some of the social difficulties in borderline personality disorder, increasing the likelihood of unpredictable behaviour with close friends and partners, and indeed with clinicians seeking to build therapeutic alliances. The operation of such a mechanism is open to further psychological (and neuroscientific) investigation, and may permit improved understanding of aetiology. As importantly, it could provide an objective focus for measuring treatment outcomes and developing more effective treatment.

6. THE ROLE OF REWARD AND LOSS IN DECISION MAKING IN BORDERLINE PERSONALITY DISORDER AND BIPOLAR DISORDER

Neuropsychological assessments also suggest that both borderline personality disorder and bipolar disorder are associated with impairments in decision-making. In borderline personality disorder, impairments have been demonstrated in delayed discounting (Lawrence et al., 2010) and decision making (Kirkpatrick et al., 2007, Schuermann et al., 2011). However, many of the instruments used are contaminated by attentional and memory demands that can complicate the interpretation of borderline personality disorder impairments while making decisions.

In bipolar disorder impaired decision-making is a diagnostic criterion of mania, implying a specific association with mood elevation. However, decision-making problems are also measurable in euthymia (Adida et al., 2011, Ahn et al., 2011, Gorrindo et al., 2005) although the findings in laboratory studies are inconsistent (Murphy et al., 2001, Rubinsztein et al., 2006) and the variety of different tasks used makes comparison between studies difficult. Mature bipolar patients also show consistent impairments in the attentional and memory domains and in tests of executive function, which inevitably complicates interpretation of deficits on complex decision-making tasks (Bourne et al., 2013).

In this study, I have tested the hypothesis that women with borderline personality disorder will have impairments in using explicit reinforcement cues

while making risky choices compared to female participants with bipolar disorder or healthy controls. I administered a task which required participants to choose to play one of two options, one with a 0.5 probability of winning or losing a fixed amount and another gamble that varied in magnitudes of gain and loss and the probabilities with which these outcomes were delivered (Rogers et al., 2003, Rogers et al., 2004, Rock et al., 2013). Variability in decision-makers' choices provides information about the attentional processing of reinforcement cues and how this influences the selection of actions based upon their normative (i.e. expected) value (Rock et al., 2013). Since the task places only minimal demands upon working memory or learning, it offers an assessment of decision-making that is independent of wider cognitive dysfunction in clinical populations.

Method

The study was funded by the Oxfordshire Health Services Research Committee and approved by the Oxfordshire NHS research ethics committee (OxRecA – 10/H0604/64). All participants gave written informed consent.

Participants

The participant groups are described in chapter 4.

Risky choice task (Rogers et al., 2003, Rock et al., 2013)

Each trial required participants to choose between playing one of two simultaneously presented gambles (Fig 6.1A). Each gamble was represented visually by a histogram, the height of which indicated the relative probability of gaining a given number of points. The possible gains were indicated in green ink above the histogram, while the possible losses were indicated in red ink underneath. On each trial, one gamble (coloured yellow) was always the control gamble, consisting of a 50% probability of winning 10 points and a 50% probability of losing 10 points. The alternative 'experimental' gamble (coloured blue) varied in the probability of winning which was either high or low, the gains which were either large or small (70 vs. 30 points) and the losses which were either large or small (70 vs. 30 points).

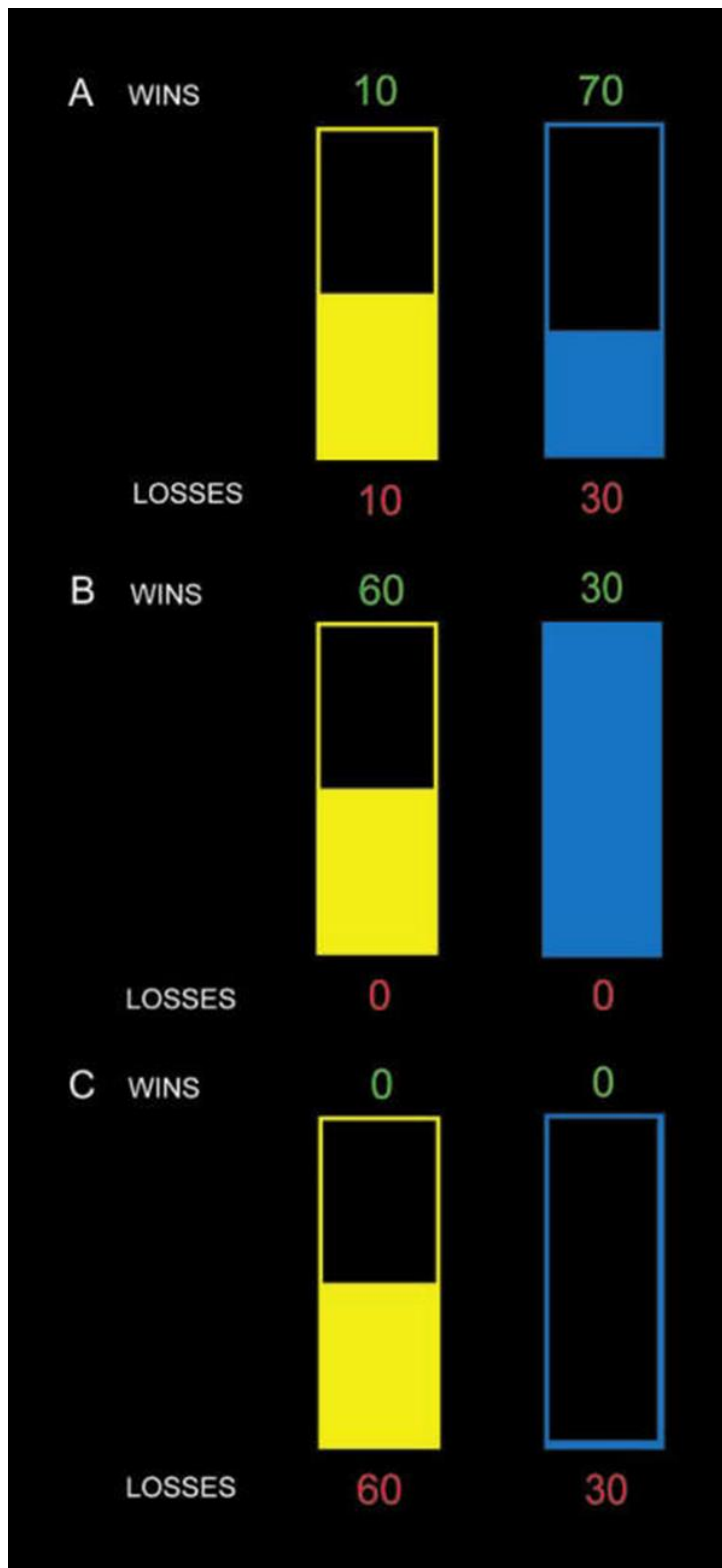


Figure 6.1. (A) Example display from the risky choice task, consisting of an 'experimental' gamble with a 40% probability of winning 70 points and a 60% probability of losing 30 points versus the control gamble with a 50% probability of winning 10 points and losing 10 points. (B) A 'gains-only trial' consisting of a certain win of 30 points and a gamble with a 50% probability of winning 60 points or 0 points. (C) A 'losses-only' trial consisting of a certain loss of 30 points and a gamble with a 50% probability of losing 60 points or 0 points.

The orthogonal combination of these variables, in a completely crossed design resulted in eight trial types with expected values that ranged between -30 and +30. The control gamble and the 'experimental' gamble appeared randomly on the left or right of the display. Participants were required to press the '1' or '2' key on a standard computer keyboard to indicate choice of the gamble presented on the left or the right.

In addition, two extra trial types were included. These represented choices between gambles known to be subject to non-normative biases of risk-aversion and risk-seeking behaviour (Kahneman and Tversky, 1979, Schneider and Lopes, 1986). The first type was 'gains only' (Fig 6.1B) in which participants were presented simultaneously with a guaranteed win of 30 points or a 50% chance of winning 60 points. Neither option offered involved any associated losses. By contrast, in the 'losses only' trial type (see Fig 6.1C), volunteers were presented simultaneously with a guaranteed loss of 30 points or a 50% chance of losing 60 points. Again, neither option offered any associated gains. For the 'gains only' and 'losses only', the dependent measure was the proportion of choices the volunteers chose the guaranteed outcome. Extensive evidence indicates that participants make risk-averse choices in the gains-only trials and risk-seeking trials in the losses only trials (Kahneman and Tversky, 1979).

All 10 trial types were presented pseudorandomly within four blocks. At the beginning of each block, participants were given 100 points, and asked to make choices that would increase this amount by as much as possible. These points had no monetary value. Visual feedback was given after each choice and the

updated points total was presented for 2 seconds before the next trial. Across the four blocks, there were eight repetitions each of the 'experimental' gambles and 'gains only' and 'losses only' trial types.

Statistics

Dependent measures of the risky choice task included (i) the proportion of choices of the experimental over the control gamble as a function of high or low probability, high or low gains, and high or low losses; (ii) choice of the experimental gamble as a function of expected value; . All data in the text, figures and tables are reported as untransformed values.

Proportionate choice and mean deliberation times were analysed using a mixed ANOVA with the between-subject factors of group and the within-subject factors of probability (high vs. low), possible gains (large vs. small), and possible losses (large vs. small). The 'gains only' and 'losses only' trials were analysed with group as the between subject factor and trial type ('gains only' vs. 'losses only') as a single within-subject factor. Proportionate choice of the experimental gamble was also analysed in an extra mixed ANOVA with the between-subject factor of group (borderline personality disorder, bipolar disorder and controls) and the within-subject factor of expected value (-30, -14, -10, -6, 6, 10, 14, 30).

Results

The clinical characteristics of the three groups are described in chapter 4.

Proportionate choice of the 'experimental' gamble (pEG).

Participants chose the experimental gamble significantly more often when the probability of winning was high compared to low ($pEG \pm SE = 0.728 \pm 0.022$ vs 0.296 ± 0.026 , $F(1,57) = 160.738$, $p < 0.001$) (Figure 6.2) and to a very similar extent across the participant groups (borderline personality disorder: $pEG \pm SE = 0.727 \pm 0.038$ vs. 0.373 ± 0.045); bipolar disorder: $pEG \pm SE = 0.764 \pm 0.038$ vs. 0.256 ± 0.045 and healthy controls: $pEG \pm SE = 0.694 \pm 0.038$ vs. 0.259 ± 0.045 $F(2,57) = 1.721$, $p = 0.188$). Participants also chose the 'experimental' gamble more often when possible gains were large as opposed to small ($pEG \pm SE = 0.567 \pm 0.022$ vs. 0.458 ± 0.017 , $F(1,57) = 28.108$, $p < 0.001$) (Figure 2). Post-hoc tukey tests indicated that borderline personality disorder participants were more likely than the other two groups to choose the experimental gamble when possible gains were low, however, this was not statistically significant ($p = 0.098$, $p = 0.067$ for bipolar and healthy control participants respectively.).

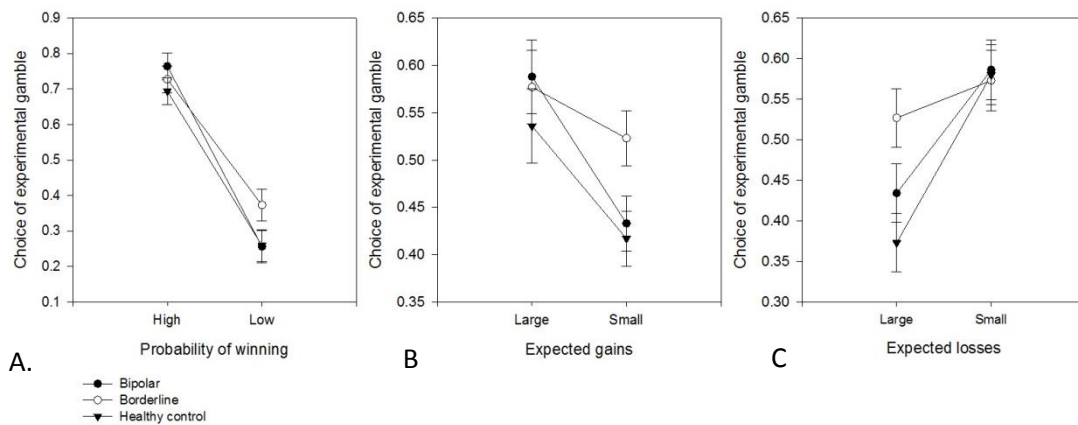


Figure 6.2. Choice of the experimental gamble at (A) high and low probabilities of winning, (B) large or small expected gains, (C) large or small losses by 20 individuals with DSM-IV borderline personality disorder, 20 (euthymic) individuals with DSM-IV bipolar disorder and 20 non-clinical healthy controls.

Participants preferred the experimental gamble significantly less frequently when possible losses were large compared to when they were small, $F(1)=30.545$, $p<0.001$) (Figure 6.2). However, this pattern of choices was significantly different between groups ($F(2,57)=3.67$, $p=0.032$). Post hoc comparisons showed that there were significant differences between the borderline personality disorder participants and healthy control groups in their choice of gambles with large losses ($pEG \pm SE = 0.5266 \pm 0.039$ vs. 0.3734 ± 0.030 , $p=0.010$), and low potentials gains ($pEG \pm SE = 0.523 \pm 0.030$ vs. 0.0417 ± 0.031 , $p=0.033$). No significant differences in the choice of the experimental gamble were found between bipolar disorder and healthy control participants.

Probability of winning	Possible gains	Possible losses	Expected Value*	Borderline pEG±SE	Bipolar pEG±SE	Healthy control pEG±SE	MD, 95% CI
High (0.60)	Large (70)	Large (70)	14	0.73 (0.06)	0.81 (0.04)		-0.08, 0.19
				0.73 (0.06)		0.64 (0.07)	0.81, 0.53
					0.81 (0.04)	0.64 (0.07)	0.163, 0.19
		Small (30)	30	0.74 (0.04)	0.87 (0.06)		-0.13, 0.16
				0.74 (0.04)		0.86 (0.04)	-0.12, 0.17
					0.87 (0.06)	0.86 (0.04)	0.01, 0.17
	Small (30)	Large (30)	-10	0.68 (0.04)	0.55 (0.08)		0.13, 0.12
				0.68 (0.04)		0.52 (0.07)	0.16, 0.22
					0.55 (0.08)	0.52 (0.07)	0.03, 0.22
		Small (30)	6	0.76 (0.05)	0.83 (0.04)		-0.07, 0.18
				0.76 (0.05)		0.76 (0.07)	0.01, 0.18
					0.83 (0.04)	0.76 (0.07)	0.08, 0.18
Low (0.40)	Large (70)	Large (70)	-14	0.36 (0.05)	0.26 (0.05)		0.11, 0.16
				0.36 (0.05)		0.19 (0.03)	0.18, 0.16
					0.26 (0.05)	0.19 (0.03)	0.07, 0.16
		Small (30)	10	0.48 (0.07)	0.42 (0.07)		0.06, 0.24
				0.48 (0.07)		0.46 (0.07)	0.02, 0.24
					0.42 (0.07)	0.46 (0.07)	0.04, 0.24
	Small (30)	Large (70)	-30	0.34 (0.07)	0.13 (0.04)		0.21, 0.17
				0.34 (0.07)		0.14 (0.04)	0.19, 0.17
					0.13 (0.04)	0.14 (0.04)	0.01, 0.17
		Small (30)	-6	0.32 (0.05)	0.23 (0.05)		0.09, 0.17
				0.32 (0.05)		0.25 (0.05)	0.07, 0.17
					0.23 (0.05)	0.25 (0.05)	0.02, 0.17

*Expected values for the experimental gambles equal the sum of gains and losses, weighted by their probabilities of occurrence, varying between -30 and 30, with a mean of 0. BOLD typeface indicates experimental gambles with low positive (+6) or low negative (-6) expected values, in which proportionate choice departs from linear pattern.

Table 6.1. Proportionate choice of 8 trial types of 'experimental gambles ($pEG \pm SE$) resulting from orthogonal combination of 2 levels of probability, magnitude of possible gains and losses in a risky choice task administered to 20 individuals with DSM-IV borderline personality disorder, 20 (euthymic) individuals with DSM-IV bipolar disorder and 20 non-clinical healthy controls.

Deliberation times

All participants were faster to make their choices when the potential gains were large compared to small (2297 ± 193.325 vs. 2168 ± 187 ms; $F(2,57)=9.844$, $p=0.003$). The odds of winning and different sized potential losses, by contrast had no significant impact overall upon deliberation times. Overall, there were no significant differences in deliberation times between groups (2247 ± 253 vs. 2488 ± 446 vs. 1963 ± 188 ms for borderline personality disorder, bipolar disorder and healthy control respectively) ($F(2,57)=0.641$, $p=0.531$).

	Probability of winning		Size of possible gains		Size of possible losses	
	High	Low	Large	Small	Large	Small
Borderline personality disorder	2269 ± 332	2226 ± 335	2189 ± 325	2306 ± 335	2254 ± 359	2240 ± 304
Bipolar disorder	2526 ± 332	2449 ± 335	2434 ± 325	2541 ± 335	3514 ± 359	2462 ± 304
Healthy Control	1940 ± 332	1986 ± 335	1882 ± 325	2044 ± 335	1970 ± 359	1956 ± 304

Table 6.2. Mean deliberation times (ms $\pm$ SEM) 20 individuals with DSM-IV borderline personality disorder, 20 (euthymic) individuals with DSM-IV bipolar disorder and 20 non-clinical healthy controls, as a function of high vs low probability of winning, large vs. small gains and large vs. small losses.

Proportionate choice of the experimental gamble as a function of the expected value.

Across all group the proportionate choice of the experimental gamble increased with the expected value. Choices of the experimental gamble diminished with expected values of -6 but increased with values of +6 (Figure 6.3). This non

linearity reflects the interaction between the probability of winning, the magnitude of the gains and losses. There was a significant interaction between group and expected value ($F(7,14)=1.902$, $p=0.025$). Borderline personality disorder was associated with increased choices of gambles with negative but not positive expected values when compared to the other two groups (see figure 6.3).

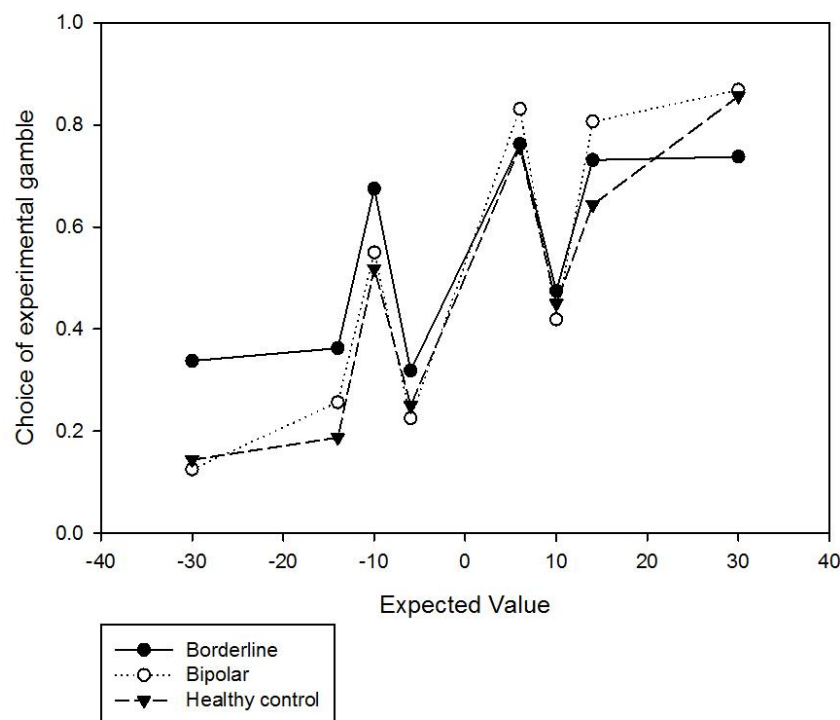


Figure 6.3. Proportion choice of the experimental gamble over the control gamble made by 20 individuals with DSM-IV borderline personality disorder, 20 (euthymic) individuals with DSM-IV bipolar disorder and 20 non-clinical healthy controls, as a function of expected value

Gains only vs. loss only trials

All participants chose the guaranteed outcome significantly more often when it was a 'gains only' compared to the 'loss only' trials ($pEG \pm SEM = 0.84 \pm 0.035$ vs. 0.19 ± 0.032 , $F(1)=142.34$, $p<0.001$). No significant differences between groups

were found in the proportion of gains only or loss only trials that were chosen ($F(1,2)=0.505$, $p=0.606$). There was a significant difference between groups in their deliberation times for wins only and loss only trials ($F(1,2)=4.276$, $p=0.019$): bipolar participants were slower to choose loss only trials compared with borderline participants and healthy controls.

	Borderline	Bipolar	HC
Prop Gain only trials (SE)	0.7563 (0.077)	0.8750 (0.050)	0.8939 (0.049)
Prop Loss only trials (SE)	0.1500 (0.047)	0.2625 (0.0634)	0.1688 (0.0539)
Gain only trials reaction times in milliseconds (SE)	2236 (350.7)	1960 (250.2)	1742 (162.7)
Loss only trials reaction times in milliseconds (SE)	2469 (330.8)	3687 (572.8)	1885 (421.5)

Table 6.3. Proportionate choices ($\pm$ SEM) of gains only or loss only trial types and reaction times (ms $\pm$ SEM) in the risky choice task administered to 20 individuals with DSM-IV borderline personality disorder, 20 (euthymic) individuals with DSM-IV bipolar disorder and 20 non-clinical healthy controls.

Discussion

Individuals with a diagnosis of borderline personality disorder exhibited significant differences in risky decision making involving explicit reinforcement cues compared to age and cognitive ability-matched participants with bipolar disorder and as well as healthy control participants. In essence, they are less sensitive to prospective losses than either comparison group. My findings

extend previous reports (Lawrence et al., 2010, Schuermann et al., 2011, Svaldi et al., 2012) in demonstrating the problems individuals with borderline personality disorder have when selecting actions and promoting decisions with negative (i.e. disadvantageous) expected values.

My findings complement evidence that impaired performance on the Iowa Gambling Task in borderline personality disorder is related to reduced EEG amplitudes when learning from negative feedback (Schuermann, Kathmann et al. 2011). Unlike the Iowa Gambling Task, the risky-choice task provides fully explicit information about the probabilities of winning as well as the magnitude of gains and losses, allowing each decision to be evaluated anew, avoiding the requirement to learn (implicitly) the likelihood of good and bad outcomes through trial and error. The impairment described here is therefore independent of any learning deficits that may also be present.

Risky behaviour is commonly observed in the everyday lives of borderline patients and problems with using reinforcement cues to identify bad outcomes may be one underlying mechanism. However, it is common to attribute, or at least associate, risky behaviour with either high trait aggression or increased impulsivity. In my relatively small sample of participants, neither AQ hostility scores nor impulsivity scores were associated with the proportion of high loss gambles chosen in any of the three participant groups, and the bipolar disorder participants were indistinguishable from the healthy controls in this respect despite elevated scores on the hostility sub-scale of the AQ and BIS-11. Thus, heightened hostility and impulsivity were not necessarily linked to altered

patterns of choices in this experiment. However, such correlations need to be interpreted with caution given the small sample size. This is also true for other significant mood symptoms, as all groups had HAMD and YMRS scores of less than 7. Nor can the results be attributed to differences in general intelligence, as these were matched across all 3 groups, and the borderline participants made their decisions at speeds comparable to other groups, ruling out the possibility of generalised motivational deficit.

Effective decision making involves registering and assimilating information from multiple sources; in this instance, the probabilities of favourable outcomes, the magnitudes of the gains, and the magnitude of any losses. Previously, it has been shown that male prisoners with borderline personality disorder opted for choices with high probabilities of reward regardless of the magnitude of potential losses (and did so even in circumstances when offered the opportunity to avoid any decision at all) (Kirkpatrick et al., 2007). The present findings demonstrate problems in the use of reward signals in a community sample of females with borderline personality disorder, indicating that there may be similarities (Lieb et al., 2004, Johnson et al., 2003) in the mechanisms underlying the diagnoses.

Extensive neuropsychological evidence points to a role for the orbitofrontal cortex, the ventromedial cortex and limbic structures in risky decision-making, reflecting their importance in the representation of value (Levy et al., 2012) and the use of choice feedback (Bechara, 2003). Borderline personality disorder has also been found to be associated with reduced anterior and posterior cingulate

grey matter volume (Hazlett et al., 2005) structures which have been shown to represent the magnitude of gains and losses in the same risky choice task used here (Rogers et al., 2004). However, other data indicate broader patterns of neuropsychological dysfunction in borderline personality disorder, including those associated with dorsolateral prefrontal areas and related limbic systems (Bazanis et al., 2002, Ruocco, 2005). Therefore, the neural basis for the neuropsychological profile in borderline personality disorder remains uncertain and not yet understood.

In contrast to the borderline personality disorder participants, the bipolar group did not differ from controls. Increased salience of gains has been reported in bipolar disorder using an Iowa gambling task paradigm (Brambilla et al., 2012). Reduced sensitivity to emotional contexts that highlight rewards or punishments have been described in young unmedicated bipolar disorder II/NOS, possibly reflecting changes in risk attitudes (Chandler et al., 2009). However, I found no evidence that the mature bipolar disorder patients studied here, nor the borderline personality disorder participants, showed changes in shifts between risk-averse and risk-seeking choices for gains and losses respectively (Schneider and Lopes, 1986).

Both clinical groups were taking psychotropic medications, with an excess of antidepressant (predominantly SSRIs) treatment in the borderline personality disorder group and it is possible that antidepressants influence risky choice (Del-Ben et al., 2005). Possible alterations in the serotonergic system in borderline personality disorder have been inferred from small genetic

association studies (Maurex et al., 2009, 2010), so an interaction between an abnormal serotonergic system and SSRI effects cannot be excluded. However, more generally, the absence of differences in speed of performance is also against non-specific effects of other medications. Serotonin has also been implicated in decision making, although the literature remains limited (Rogers, 2011). In healthy controls, tryptophan supplements were associated with *increased* sensitivity to losses (especially associated with small gains) (Murphy et al., 2009) and a marked and significant diminution of the reflection effect (the asymmetric pattern between loss-only and gain-only choices).

These are *opposite* effects to those seen here, and tryptophan might be expected to have the same direction of effect as that of SSRIs. Overall, SSRIs seem very unlikely to explain what I observed here. On the contrary, SSRIs might act to correct the decision-making deficits seen in borderline personality disorder. The literature on their clinical benefits in borderline personality disorder is surprisingly limited, although American clinical guidelines support their use primarily in patients with affective dysregulation, seeming to suggest an effect primarily on mood (American Psychiatric Association, 2001). The positive trial by Rinne et al (2002) targeted depressive symptoms, a smaller study (Salzman et al., 1995) described changes in anger ratings, while an even smaller study (Simpson et al., 2004) found no benefit from adding fluoxetine after completion of a behavioural psychotherapy. The finding of specific and measureable cognitive deficits means that, rather than conventional clinical trials, experimental medicine may provide a smaller scale methodology to explore medicines and psychological interventions more efficiently for borderline

personality disorder. Positive treatment benefits in turn will allow a weighing of how much different neurocognitive mechanisms contribute to psychopathology.

In this chapter I have demonstrated that borderline personality disorder, but not bipolar disorder, is associated with impaired decision making and, specifically, problems using reinforcement cues to identify optimal choices. These problems are unlikely to reflect primary impairments in learning, memory or executive failures. Difficulties in using reward information to make decisions are likely to impair day-to-day function. Such deficits are consistent with the clinical presentation of borderline personality disorder where persistent engagement in harmful and risky behaviours is often prominent. They add to the developing picture of how borderline personality disorder emerges as a clinical syndrome from its underlying substrate of specific cognitive impairments. Such impairments offer new targets for treatments facilitating behavioural change in borderline personality disorder.

7. ENHANCED POST-ERROR SLOWING IN BORDERLINE PERSONALITY DISORDER COMPARED TO BIPOLAR DISORDER AND HEALTHY CONTROLS

Impulsivity is a prominent feature of both bipolar disorder and borderline personality disorder. It is manifest in a number of problematic behaviours associated with the two conditions, including self-harm or drug and alcohol misuse (Grant et al., 2008, Haw et al., 2001, Cassidy et al., 2001).

Neurocognitive assessments have shown that individuals with a diagnosis of borderline personality disorder exhibit elevated impulsivity in the motor domain (i.e. withholding of certain actions), cognitive domain (i.e. withholding decisions in order to sample sufficient information), and temporal discounting (i.e. foregoing small immediate rewards to secure larger delayed rewards) (Dougherty et al., 1999, Lawrence et al., 2010). This heightened impulsivity significantly complicates treatment intervention, and is associated with worse clinical outcomes in individuals with either diagnosis.

While the centrality of impulse control problems in the experience and presentation of borderline personality disorder is widely acknowledged (Sebastian et al., 2013, Peters et al., 2013), much less is known about other forms of sensori-motor performance, for example, in speeded tasks. A major question remains whether and how aspects of sensori-motor function and its efficiency are impacted by the central features of the diagnosis. Behavioural control involves balancing the speed and accuracy of motor responses in order to avoid mistakes that might be costly in cognitive or emotional terms (Heitz and

Schall, 2012, Forstmann et al., 2010). The clinical characteristics of borderline personality disorder suggest that balancing speed and accuracy will be impaired.

One central feature of sensori-motor control is the ability to adjust behaviour following mistakes (Yeung and Summerfield, 2012). Typically, people tend to slow their responses once they have made an error in so-called post-error slowing, presumably in order to recover and improve their future performance (Dutilh et al., 2012, Laming, 1979, Rabbitt, 1967). To date, little is known about whether such post-error processing, and performance recovery, is disturbed in borderline personality disorder (Ruchow et al., 2006, de Bruijn et al., 2006a), despite its relevance to understanding emotional regulation and resilience in affected individual.

Current models of speeded decision-making posit response 'accumulators' that sample information over time ('drift rate') and integrate this evidence until a 'boundary' condition is reached and the response is then performed (Yeung and Summerfield, 2012, Ratcliff and McKoon, 2008).

From the perspective of these 'drift-diffusion' models, post-error slowing is most typically attributed to heightened response caution, reflected in upward adjustments in boundary conditions for available responses. However, in principle, post-error slowing could also involve a bias away from erroneous

responses, reflected in reduced starting values of accumulators, distraction reflected in lower drift-rates, or non-specific delays in the commencement of information sampling (Dutilh et al., 2012). In this experiment, I used a simplified drift-diffusion model – the EZ model (Wagenmakers et al., 2007) – to investigate post-error slowing in a sample of individuals with diagnoses of borderline personality disorder compared to age and cognitive ability-matched bipolar disorder and controls participants.

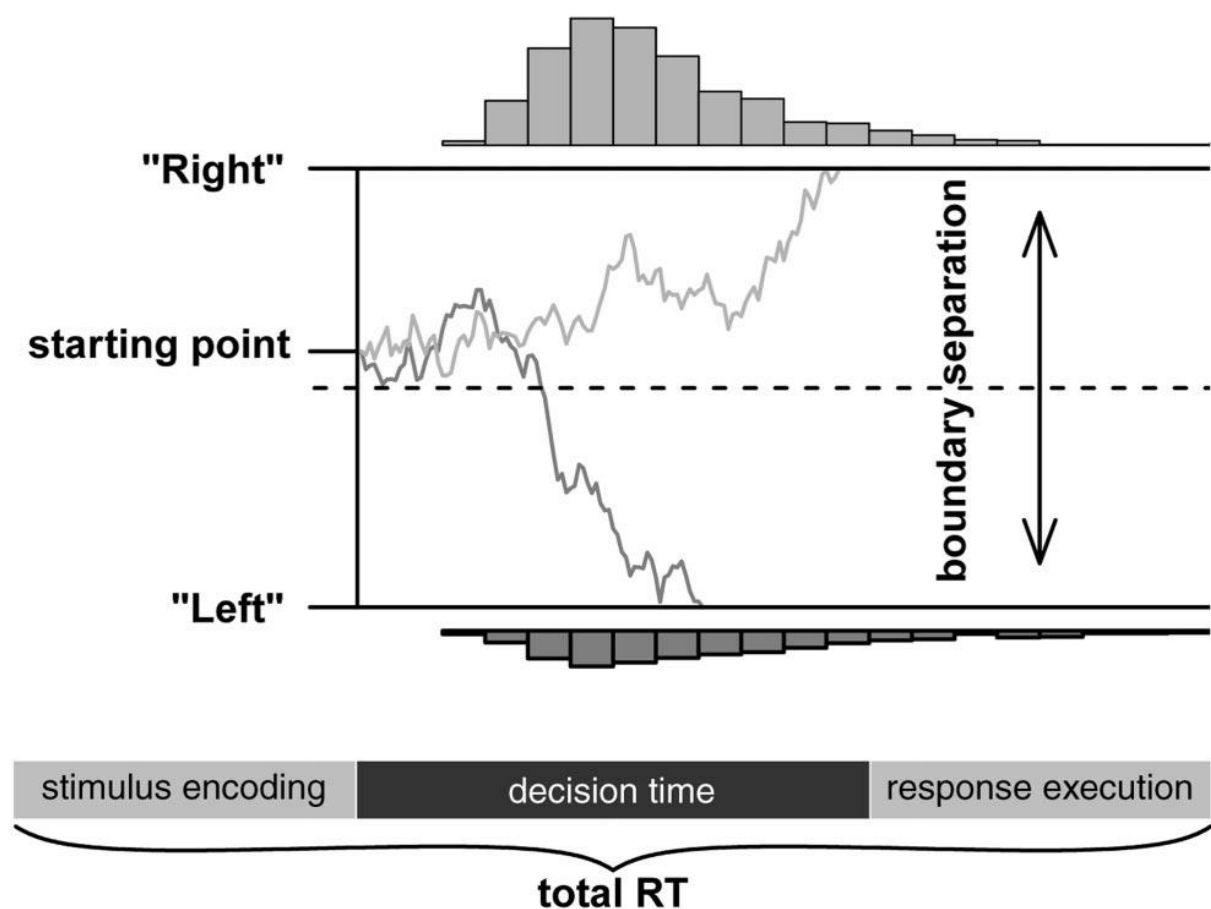


Fig 7.1. The EZ diffusion model and its parameters (from Dutilh et al 2013). Graphical illustration of the EZ diffusion model.

The EZ-diffusion model is an implementation of a drift-diffusion approach that is suited to the examination of individual and experimentally-manipulated differences in drift and boundary parameters (Van Ravenzwaaij and Oberauer,

2009). It determines drift rate v , boundary separation a , and non-decision time T_{er} from the mean reaction time (MRT), the variance of the mean reaction time (VRT), and the proportion of trials that were answered correctly (P_c). Thus, the model transforms the observed variables into three unobserved variables, allowing statistical analysis to be conducted on the latent rather than observed variables. This is advantageous since the latent variables all have clear psychological interpretation. The drift rate (v) represents the speed of information uptake; the boundary separation (a) is a measure of response caution and non-decision time (T_{er}) the time spent on irrelevant processes. The model was applied to the entire data set.

I used a simple two-choice reaction-time task in which two stimuli were mapped unambiguously to one of two motor responses. The task instructions emphasised speed of responding to achieve an explicit pre-instructed error rate. Participants were told to respond as quickly as possible and that an error rate of 10% was acceptable. Comparison of the borderline personality disorder and bipolar disorder participants enabled any shared associations between altered post-error slowing and shared features of these illnesses (e.g. heightened impulsivity) to be explored.

Method

The study was funded by the Oxfordshire Health Services Research Committee and approved by the Oxfordshire NHS research ethics committee (OxRecA – 10/H0604/64). All participants gave written informed consent.

Participants

The participant groups are described in chapter 4.

Choice reaction task

On each trial, one of 2 symbols (X or O - see figure 7.2) was presented in white on a black background. Participants were instructed to press one of two buttons, with the index finger of their left or right hand, in response to each symbol respectively. Symbols were presented until the participant responded. There was a 500-ms interval between trials when a blank screen was shown. Participants were instructed to respond as quickly as possible. If they responded incorrectly a beep sounded. At the end of each block of 40 trials, a feedback screen indicated the error frequency and mean reaction times for that block. Participants completed 6 blocks of 40 trials.

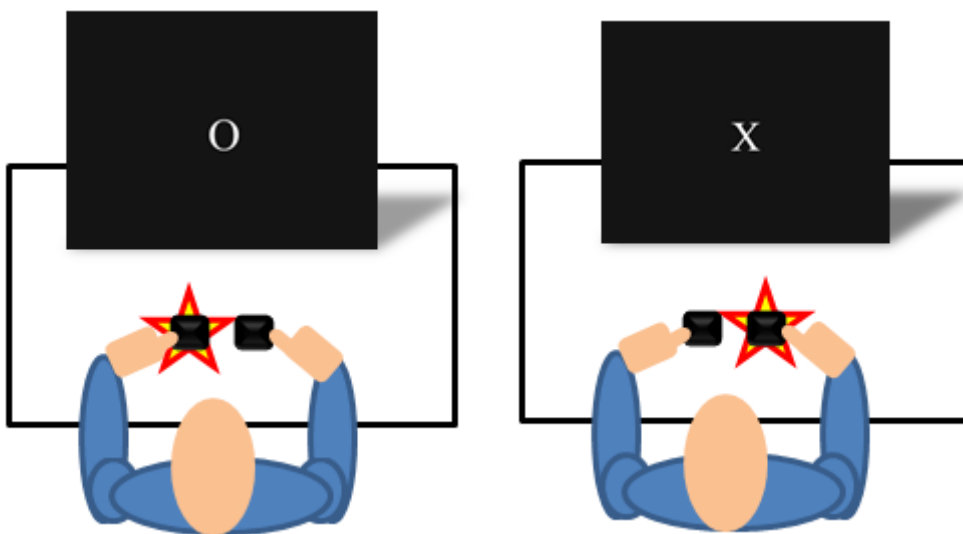


Fig 7.2 Choice reaction task

Statistics

Mean reaction times for correct trials and error trials (and proportionate error rates) were initially analysed by ANOVA with the single-factor of group. Error rates were arcsine transformed as is necessary whenever variances are proportional to means (Howell, 1987). We then applied the EZ diffusion model to all trials in the dataset. The parameters: drift rate, boundary separation and non-decision time were compared between groups using ANOVAs.

Post-error slowing (PES) was tested by comparing RTs and errors on immediately post-error trials with immediately pre-error correct trials as described by Dutilh et al (2012). The most popular way to quantify PES is to compare trials that follow errors with those that follow correct responses. However, this approach is vulnerable to being confounded by longer-term changes in behaviour over the course of an experiment. For example, if participants' motivation wanes as the experiment progresses, responses become slower and less accurate. Since most correct trials will be in the early part of the game when motivation was higher whereas error trials will be in the later part of the experiment, any calculation that compares post-correct and post-error will tend to overestimate the PES even if real post error slowing was absent (Dutilh et al., 2012). Conversely, if a participant is initially very slow but highly accurate, but then become faster and less accurate as the experiment progresses, PES may be underestimated. Here, I adopted the technique proposed by Dutilh et al (2012) to quantify PES as the difference in RT between post-error and associated pre-error trials.

Results

The clinical characteristics of the three groups are described in chapter 4.

Behavioural results

Overall, there was no significant difference in overall mean reaction times between the three groups (372ms vs 342ms vs 343ms for borderline personality disorder, bipolar disorder and healthy controls respectively $F(2,57)=1.683$, $p=0.195$). No between group differences in correct (376ms vs 346ms vs 347ms for borderline personality disorder, bipolar disorder and healthy controls respectively ($F(2,57)=1.787$, $p=0.177$) or error trial reaction times (329ms vs 321ms vs 302ms for borderline personality disorder, bipolar disorder and healthy controls respectively $F(2,57)=0.518$, $p=0.598$) were found. There were no significant differences in the proportion of errors between the three groups (0.084 vs 0.071 vs 0.071 for borderline personality disorder, bipolar disorder and healthy controls respectively, $F(2,57)=0.617$)).

SAEZ model results

The three groups had significantly different drift rates (.231 vs .289 vs .307 for borderline personality disorder, bipolar disorder and healthy controls respectively (see Figure 7.3), $F(59)=6.07$, $p=0.004$). Post-hoc tukey tests indicated that borderline personality disorder was associated with lower drift rates compared with bipolar disorder ($p<0.05$) and healthy controls ($p<0.05$). Significant group differences in boundary separation (114 vs .099 vs .092 for

borderline personality disorder, bipolar disorder and healthy controls respectively, $F(59)=4.45$, $p=0.021$) and non-decision times were also observed (.138 vs .188 vs. .179, $F(59)=4.5$, $p=0.015$). Post-hoc tukey tests indicated that borderline personality disorder was associated with greater boundary separation than healthy controls ($p<0.05$), and shorter non decision times compared with healthy controls ($p<0.05$) No significant differences were observed between bipolar participants and healthy controls.

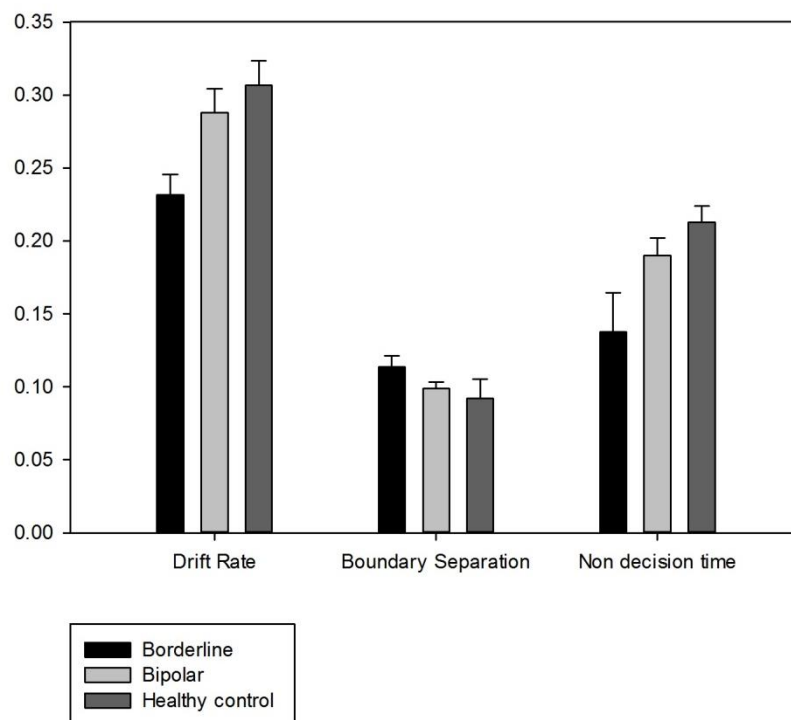


Figure 7.3. EZ diffusion model parameters for all trials in 20 individuals with DSM-IV borderline personality disorder, 20 (euthymic) individuals with DSM-IV bipolar disorder and 20 non-clinical healthy controls in a simple choice reaction task.

Post error slowing

Overall, the pattern of mean RTs and error rates preceding and following errors is illustrated in Figure 7.4. Following Dutihl et al (2012), PES, estimated as the difference between mean reaction times on the immediately post-error trials compared to pre-error trials (see Figure 7.5), differed significantly between groups (PES (ms $\pm$ SEM) = 412.21 $\pm$ 81.40 vs 208.42 $\pm$ 28.50 vs 157.65 $\pm$ 33.03 for borderline personality disorder, bipolar disorder and healthy controls respectively, $F(2,57)= 6.598, p=0.003$). This slowing was not associated with any differences in the proportion of errors made in the trial following an error ($F(2,57)=0.098, p=0.907$). Post-hoc tukey tests indicated that PES was significantly greater in borderline participants compared with bipolar participants ($p<0.05$) and healthy controls ($p<0.05$). No significant between group differences in the proportion of errors in the trial following an error were observed in pairwise post-hoc comparisons ($p>0.05$).

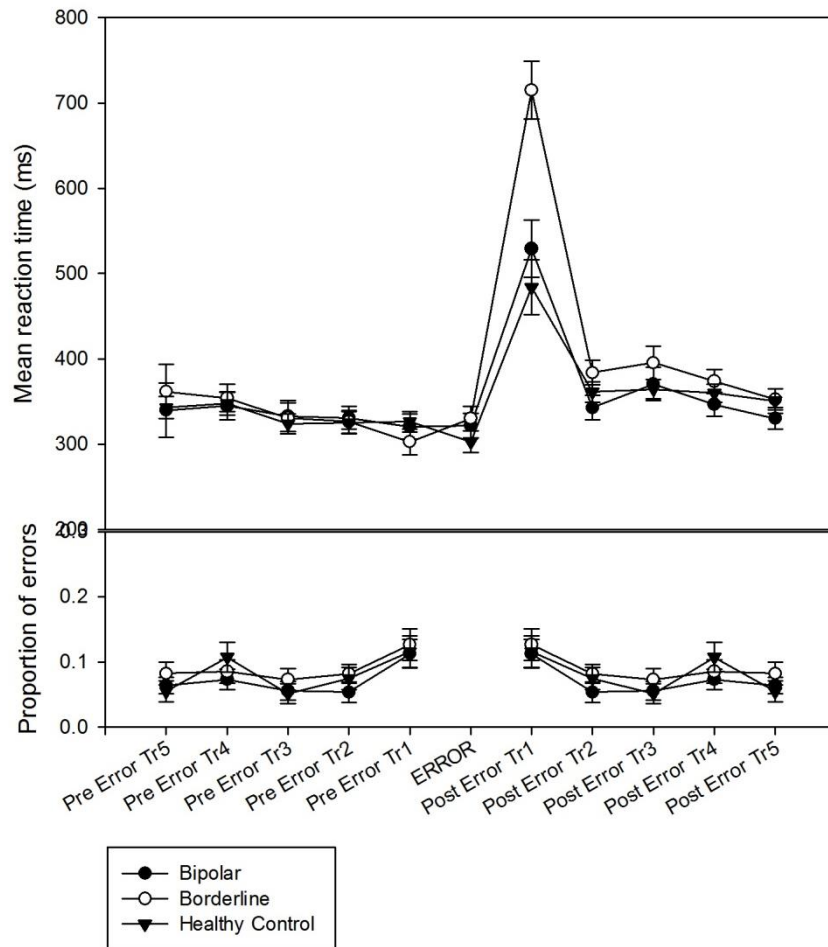


Figure 7.4. Reaction times and proportion of errors for the 5 trials preceding an error, the error trial and the 5 trials following an error in 20 individuals with DSM-IV borderline personality disorder, 20 (euthymic) individuals with DSM-IV bipolar disorder and 20 non-clinical healthy controls in a simple choice reaction task.

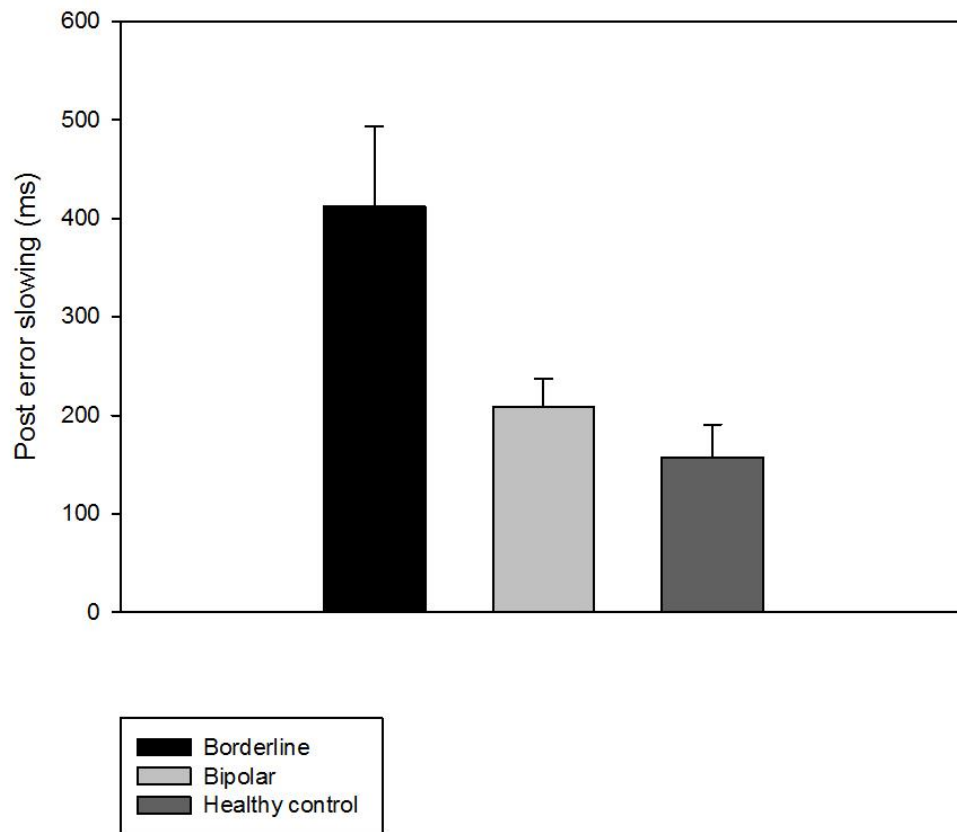


Figure 7.5. Post error slowing in 20 individuals with DSM-IV borderline personality disorder, 20 (euthymic) individuals with DSM-IV bipolar disorder and 20 non-clinical healthy controls in a simple choice reaction task.

Across all three groups there was no significant correlation between impulsivity as measured using the BIS and MRT, proportion of correct responses, or any of the EZ variables. In the bipolar disorder group, there was a significant correlation between the proportion of correct responses and BIS ($r = -0.492$, $p = 0.028$). In the HC group there was a near significant correlation between MRT and BIS ($r = 0.437$, $p = 0.054$). No significant correlations between BIS and any other variables were found in the borderline personality disorder group. Post-

error slowing was not correlated with impulsivity as measured using the BIS in any of the three groups ($r=.290$, $p=0.214$, $r=-.108$, $p=0.650$, $r=-.246$, $p=0.295$ for borderline personality disorder, bipolar disorder and healthy controls respectively) and impulsivity did not significantly contribute to the group differences in PES. These remained significant when the ANOVA was repeated using the BIS as a covariate ($F(2,57)=5.66$, $p=0.006$).

Discussion

These data show that there was no overall difference between the groups in terms of reaction times for correct responses or error responses or in the proportion of errors. A well validated EZ drift-diffusion model; (Wagenmakers et al., 2007) found shorter drift rates, longer boundary separation and shorter non-decision times in borderline personality disorder compared to bipolar disorder and healthy controls. In addition, post-error slowing was significantly greater in borderline personality disorder participants than in those with bipolar disorder or healthy controls.

Some of these findings are consistent with those of Ruchow et al (2006) who found no difference in mean reaction time for correct or error trials or in proportion of errors when comparing a borderline personality disorder group with healthy controls using a go/no-go task. However, they are inconsistent with Rentrop et al's (2008) report of fast responses and more errors when comparing an inpatient borderline personality disorder group to healthy controls

using an auditory go/no-go paradigm. The inconsistency may relate to task demands or complexity, or a specific deficit in response inhibition as Rentrop et al's findings were limited to nogo blocks (which are more complex than go blocks and require response inhibition).

Notwithstanding these discrepancies, the EZ model results indicate that borderline personality disorder is associated with slower uptake of information (drift rate), more cautious responding (boundary separation) and less time spent on irrelevant processes (non-decision time).

Several explanations have been proposed to account for PES (Dutilh et al., 2012). These include increased response caution (that an error prompts individuals to accumulate more information before making a following decision) (Rabbitt and Rodgers, 1977), a priori bias (that people become negatively biased against the response option that just resulted in an error) (Rabbitt and Rodgers, 1977), decreased variability in bias (that an error leads individuals to more accurately control the timing of the onset of information accumulation) (Laming, 1979), distraction of attention (that an error is an infrequent and surprising event) (Notebaert et al., 2009), or delayed startup (that an error delays the start of evidence accumulation because individuals need time to reassess their own performance level and overcome disappointment (Rabbitt and Rodgers, 1977). Using data from a 1,094,886 trial lexical decision task, Dutilh et al (2012) have demonstrated that increased response caution is thought to almost exclusively account for post-error slowing in healthy volunteers. They suggest that PES can be explained in terms of self-regulation

processes and cognitive control: that is, individuals alter response thresholds by speeding up after each correct response and becoming more cautious after every error.

In principle the increased PES seen in the borderline personality disorder participants might involve any of the above; however, I tentatively suggest that it reflects increased caution following an error compared to that in individuals with bipolar disorder or healthy controls; and that the absence of any difference in the proportion of errors or distribution of errors following an error suggests that the increase in response caution is necessary to maintain performance in the borderline personality disorder group. Rentrop et al (2008) found that borderline personality disorder was associated with an absence of speed-accuracy trade off (no compensatory slowing was observed in order to reduce errors) in a go/nogo task when compared to healthy controls. They suggested that this related to an involuntary reaction style. My findings, in a 2-choice reaction time, refute this assertion and suggest instead that individuals with borderline personality disorder slow down more than bipolar disorder or healthy controls to maintain accuracy.

The absence of any correlation with impulsivity as measured by BIS scores and MRT or error rate in the borderline personality disorder group is consistent with some studies (Stevens et al., 2004, Rentrop et al., 2008, Horn et al., 2003) but not others (Bazanis et al., 2002). Bazanis et al demonstrated that impulsivity was associated with slower decision times in borderline personality disorder. In

healthy participants. Dickman et al found that there was little correlation between high impulsivity and response execution and accuracy (Dickman and Meyer, 1988). However, given the small sample sizes of the majority of these studies (and in the findings presented here) correlations need to be interpreted with caution.

Post error adjustment is likely to draw upon regions in the anterior cingulate and lateral prefrontal cortex (Van Veen and Carter, 2002). Structural fMRI studies have found that borderline personality disorder is associated with reduced anterior cingulate volumes (Hazlett et al., 2005), and reduced activity in this area has been observed under conditions of behavioural inhibition in the context of negative emotion (Silbersweig et al., 2007).

Limitations

The low number of error trials across the task in all groups meant that I was unable to compare the EZ model parameters for pre and post error trials as suggested in Dutilh et al (2012). All error trials were followed by feedback in the form of a beep which may have distracted participants. However, given that the error frequencies did not differ between groups, the increased caution in the borderline personality disorder group is likely to be a true phenomenon. Given that the only significant between group differences were on the first trial following an error it seems likely that the differences observed in the EZ parameters are predominantly accounted for by the post error trials. I was

unable to compare the pre and post error trials as there were too few errors to allow the model to be applied.

The two clinical groups were taking psychotropic medication. Most psychotropic medication is associated with slower reaction times however I did not find any evidence of between group differences in mean reaction times. The two clinical groups were broadly matched in terms of psychotropic medication with the exception of antidepressants (see chapter 4). In healthy volunteers one off doses of SSRIs have been shown to impair reaction times in a variety of neuropsychological tests but the results from multiple dose studies in healthy volunteers are more inconsistent (Serretti et al., 2010). In depressed patients improvements in performance are often noted (Culang et al., 2009). The impact of SSRIs on reaction times in borderline personality disorder is unknown so I cannot rule out the possibility that the higher use of SSRIs in the borderline personality disorder group is a confounding factor.

8. CONCLUSIONS AND FUTURE DIRECTIONS

The findings outlined in this thesis address the diagnostic challenge posed by bipolar disorder and borderline personality disorder from two perspectives: the nature of current clinical practice, and how cognitive science can assist in objectively distinguishing the two disorders.

Clinical practice

The majority of clinicians agree that borderline personality disorder and bipolar disorder can be difficult to differentiate because of overlapping diagnostic criteria and a reliance on self-reported symptoms. Despite acknowledging this diagnostic difficulty the majority of clinicians continue to make diagnoses.

Clinical diagnostic practice as revealed in the present study is not adequate to differentiate reliably bipolar disorder or borderline personality disorder. It is ironic that a preoccupation with diagnosis is attributed to psychiatrists by those critics who hold the minority view that diagnosis is invalid and therefore without value for psychiatric patients (The British Psychological Society, 2013). In fact, psychiatrists may be too intent on being sympathetic and searching after meaning, to the detriment of their role as diagnosticians.

Psychiatrists in training are taught the distinctions between the major diagnostic categories and the need for systematic interviewing. A large number of structured and exhaustive research interviews have been developed which have long been recognised in research settings to improve inter-rater reliability.

All require the interviewer to ask the same questions in the same way with every patient. While this approach may be known in theory by almost all psychiatrists, and systematic enquiry is recommended in some guidelines, there is no obligation for psychiatrists actually to follow this methodology in their practice. Accordingly, it would be surprising if they did. But if they do not, they risk failing to add value to patient assessment and diagnosis.

Most psychiatrists know what diagnostic criteria contribute to diagnosis, so a change in application of this knowledge may be what is required. Information technology offers obvious opportunities for systematically enhancing data collection and diagnosis. Almost every administrative detail of the patient journey is currently better collected by existing software than clinical information that would facilitate reliable diagnosis.

The lack of robust diagnoses in clinical practice has widespread implications. Patients may be denied necessary treatments, or receive unnecessary or inappropriate treatments leading to longer periods of illness and poorer prognosis. Misdiagnoses in clinical practice may lead to inappropriate services being developed and inadequate resources in certain disease areas. From a research perspective, case registries compiled from such data will be less useful than previously thought as the majority rely on clinical diagnoses. I believe these findings represent a major challenge to the fundamentals of current psychiatric practice. The costs of secondary psychiatric care have ballooned in the last decade (from £4.1 billion in 2001 to £6.63 billion in 2012

(Department of Health, 2012)) arguably in advance of an understanding of what services were worth. GPs now commission services and are likely to expect psychiatrists to add value through expert assessment. A concerted effort to improve current practice seems to be required for that role and would be in everyone's interest.

Diagnosis is subject to entirely external and arbitrary factors relating to service provision, cost and stigma. In a private healthcare system, there may be incentives to select an unnecessary diagnosis or the most expensive treatment for patients. In a socialized system such as the NHS, the incentive may be to avoid rating difficult patients as requiring an intervention, and this could be particularly tempting in diagnostic groups like borderline personality disorder where it is possible to manipulate treatment thresholds or where a significant degree of clinical discretion exists (Miraldo et al., 2006)

In summary the distinctions between bipolar disorder and borderline personality disorder may be inherently difficult to make because of the overlap in how patients present in crisis, and in some symptom dimensions. If diagnosis is to be useful, it must be based on operationalised criteria and the accurate identification of symptoms and experiences. Psychiatrists are clearly trained to make diagnoses and generally know the diagnostic criteria. However the work of this thesis suggests that their practice fails to pose the right range of questions to identify either mania or borderline symptoms. The solution appears to lie in improved education and practice, perhaps facilitated by increased use of software.

Cognitive test battery

The findings from the cognitive test battery firmly support the hypothesis that bipolar disorder and borderline personality disorder are distinct disorders. The two disorders can be distinguished on the basis of their social behaviour, risky decision making and specific sensori-motor measures. The extent to which the neuropsychological findings in this thesis are trait markers or a consequence of borderline personality disorder is unclear. Further studies with high-risk individuals (such as those first degree relatives of those with bipolar disorder, or adolescents presenting with repeated self-harm) are necessary to determine this.

These findings are largely consistent with the clinical presentation of euthymic bipolar-I disorder and borderline personality disorder. The findings also illustrate a specific pattern of deficits present in borderline personality disorder which warrant further exploration. The deficits may also provide a potential treatment target and outcome measure. One of the challenges in psychotherapy is how to best measure outcomes, given that the majority of self-report measures are vulnerable to the short term impact of therapy ending, and the enhanced insight associated with a good therapeutic outcome. Laboratory tasks such as those employed here may provide a potential solution to this problem. They may also have a role in predicting treatment engagement and response.

Social function

Social dysfunction is a prominent and pervasive feature of borderline personality disorder which tends to persist despite other symptoms diminishing (Gunderson et al., 2011a). Mentalisation (the ability to understand the mental state of oneself and others) is impaired in borderline personality disorder, and there is an increasing evidence base in favour of mentalisation based therapy (MBT) (Bateman and Fonagy, 2004, 2008, 2010). Mentalising allows us to understand and interpret the behaviour of others, and deficits have been linked to the failure or disruption of early attachments (Fonagy, 2003) (as is frequently experienced in borderline personality disorder). The observations presented in Chapter 5, that participants with borderline personality disorder were unable to establish or maintain cooperative behaviour, is consistent with this theory.

In real life decisions rarely involve a simple interaction with one individual and even when they do such decisions involve a variety factors in addition to that of monetary reward, for example, expectation of future interaction, benevolence or a desire to comply with social norms. Other evidence suggests that good recovery from psychological illnesses such as depression can depend upon group-based support involving family, clubs or group-based activities (Joiner et al., 2002, Isaac et al., 2009). Behaviour in group contexts can be studied in laboratory settings using task collectively known as public goods games. These involve multiple players and allow us to explore how individuals prioritise their own interests over the interests of the group as a whole, and how they respond to the selfish behaviour of others. This is of particular interest in

borderline personality disorder as the most effective treatment modality is that of group psychotherapy in the form of therapeutic communities. To date no-one has systematically studied the responses of individuals with borderline personality disorder in a group context or which factors are most influential. Enhancing understanding of group behaviour may assist in identifying why group treatments are particularly effective, and may also guide potential psychological treatment targets.

Insensitivity to rewards and losses in risky decision making

The findings presented are consistent with the clinical picture of borderline personality disorder and represent an important treatment target given the impact of poor decision making has on patients' lives. However, decision making is a complex process and may be impaired via a number of different mechanisms. Deficits are found in a wide range of neuropsychiatric disorders. Delineating the underlying mechanism in borderline personality disorder is complicated by the high levels of impulsivity in this group. The relationship between impulsivity and poor decision making and the behavioural manifestations of this are made even more difficult by the vagueness of their definitions and the number of different cognitive and behavioural components involved. Neuroimaging and findings from lesion data suggest that the cognitive components of decision making are associated with the prefrontal cortex (PFC), an area implicated in borderline personality disorder. Maturation of the PFC may not be complete until the mid-20s i.e. after the age of onset of borderline personality disorder. Unlike healthy controls in whom impulsivity and risk taking

associated with adolescence has resolved, these deficits persist in borderline personality disorder. Understanding how the nature of these maturational changes may differ from healthy controls may provide insights into the putative mechanism for the poor decision making in borderline personality disorder.

Sensori-motor control

The post-error slowing found in participants with borderline personality disorder was striking in its specificity. It may explain the conflicting accounts in the literature about reaction times in this group and highlights the extent to which some findings may relate to task complexity as opposed to reaction time deficits per se. While the task had no emotional component, feedback in the form of a short audible tone was received following errors. This may have heightened emotional arousal disproportionately in the borderline group which then caused slowing of the subsequent response. Further studies in the absence of feedback would be helpful in exploring this. While the temporal resolution of fMRI may not be adequate to pick up changes in brain activity associated with post-error slowing, a study using EEG / MEG to pick up event-related signals would be highly informative. Given the likely role of emotional arousal, measures of autonomic arousal such as skin conductance and heart rate would also need to be included.

Conclusion

The findings in this thesis outline a number of potential reasons for the diagnostic difficulties encountered by clinicians (and patients) and point to some laboratory findings that may assist in this differentiation. However, there is a notable absence of previous clinical, behavioural or imaging research where bipolar disorder and borderline personality disorder are directly compared. The vast majority of studies tend to make comparisons with healthy control samples, and there is a tendency to overlook axis-II comorbidity in studies of bipolar disorder. The reasons for this are likely to be multifaceted. Borderline personality disorder has long been overlooked by clinicians and researchers alike. There has been a historical reluctance for those working in psychotherapies to engage in neuroscientific studies and there has been a perception that the borderline group are likely to be difficult to recruit into research studies. Unlike bipolar disorder, borderline personality disorder has been a diagnosis that has continued to change in its diagnostic description and the emergence and acceptance of the wider bipolar spectrum is a relatively new concept.

The increasing move towards transdiagnostic approaches, for example to explore mood instability as an entity rather than in any specific diagnostic group may begin to enhance our understanding as to why two disorders with different aetiologies and prognoses can have such similar phenotypes.

In summary: bipolar disorder and borderline personality disorder are common psychiatric diagnoses which have an overwhelming impact on those who suffer from them. Improving our understanding of the underlying neurobiology of these disorders, as well as exploring the processes governing assessment and diagnosis, are twin approaches that individually and together provide potent opportunities for earlier and more effective intervention and treatment.

Appendix 1

Bipolar-I

Criterion A: A Manic, Hypomanic, Mixed, or a Major Depressive Episode.

Criterion B: There has previously been at least one Manic Episode or Mixed Episode .

Criterion C: The mood symptoms are not better accounted for by Schizoaffective Disorder and is not superimposed on Schizophrenia, Schizophreniform Disorder, Delusional Disorder, or Psychotic Disorder Not Otherwise Specified.

Criterion D: The mood symptoms in Criteria A and B are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g. hypothyroidism)

Criterion E: The symptoms must cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Bipolar-II

Criterion A: The essential features of bipolar-II disorder is a clinical course that is characterised by the occurrence of one or more major depressive episodes

Criterion B: accompanied by at least one hypomanic episode

Criterion C: The individual experiences rapidly alternating moods accompanied by symptoms of a manic episode and a major depressive episode. The presence of manic or mixed episodes precludes the diagnosis of bipolar-II disorder.

Criterion D: Episodes of substance-induced mood disorder or of mood disorder due to a general medical condition do not count toward a diagnosis of bipolar-II disorder. In addition the episodes must not be better accounted for by schizoaffective disorder and are not superimposed on schizophrenia, schizophreniform disorder, delusional disorder or psychotic disorder not otherwise specified.

Criterion E: The symptoms must cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Bipolar NOS: A Classification for Sub-threshold Symptoms

The Bipolar Disorder Not Otherwise Specified category includes disorders with bipolar features that do not meet criteria for any specific Bipolar Disorder. Examples include

1. Very rapid alternation (over days) between manic symptoms and depressive symptoms that meet symptom threshold criteria but not minimal duration criteria for Manic, Hypomanic or Major Depressive Episodes

2. Recurrent Hypomanic Episodes without intercurrent depressive symptoms
3. A Manic or Mixed Episode superimposed on Delusional Disorder, residual Schizophrenia, or Psychotic Disorder Not Otherwise Specified
4. Hypomanic Episodes, along with chronic depressive symptoms, that are too infrequent to qualify for a diagnosis of Cyclothymic Disorder
5. Situations in which the clinician has concluded that Bipolar Disorder is present but is unable to determine whether it is primary, due to a general medical condition or substance induced

Appendix 2

Borderline Personality Disorder – Alternative DSM-5 model

Proposed Diagnostic Criteria

- A. Moderate or greater impairment in personality functioning, manifested by characteristic difficulties in two or more of the following four areas:
 1. **Identity:** markedly impoverished, poorly developed, or unstable self-image, often associated with excessive self-criticism; chronic feelings of emptiness; dissociative states under stress.
 2. **Self-direction:** Instability in goals, aspirations, values or career plans
 3. **Empathy:** Compromised ability to recognize the feelings and needs of others associated with interpersonal hypersensitivity (i.e. prone to feel slighted or insulted); perceptions of others selectively biased toward negative attributes or vulnerabilities.
 4. **Intimacy:** Intense, unstable and conflicted close relationships, marked mistrust, neediness, and anxious preoccupation with real or imagined abandonment; close relationships often viewed in extremes of idealisation and devaluation and alternating between over involvement and withdrawal.

- B. Four or more of the following seven pathological personality traits, at least one of which must be (5) Impulsivity, (6) Risk-taking or (7) Hostility:
 1. **Emotional lability** (as aspect of Negative Affectivity): Unstable emotional experiences and frequent mood changes; emotions that are easily aroused, intense, and/or out of proportion to events and circumstances.
 2. **Anxiousness** (an aspect of Negative Affectivity): Intense feelings of nervousness, tenseness, or panic, often in reaction to interpersonal stresses; worry about the negative effects of past unpleasant experiences and future negative possibilities; feeling fearful, apprehensive, or threatened by uncertainty; fear of falling apart or losing control
 3. **Separation insecurity** (as aspect of Negative Affectivity): Fears of rejection by - and/or separation from - significant others with fears of excessive dependency and complete loss of autonomy.
 4. **Depressivity** (as aspect of Negative Affectivity): Frequent feelings of being down, miserable and/or hopeless; difficulty recovering from such moods; pessimism about the future, pervasive shame; feelings of inferior self-worth; thoughts of suicide and suicidal behaviour.
 5. **Impulsivity** (as an aspect of Disinhibition): Acting on the spur of the moment in response to immediate stimuli; acting on a momentary basis without plan or consideration of outcomes; difficulty establishing

or following plans; a sense of urgency and self-harming behaviour under emotional distress.

6. **Risk taking** (as an aspect of Disinhibition): Engagement in dangerous, risky and potentially self-damaging activities, unnecessarily and without regard to consequences; lack of concern for one's limitations and denial of the reality of personal danger.
7. **Hostility** (as aspect of antagonism): Persistent or frequent angry feelings; anger or irritability in response to minor slights and insults.

Appendix 3

Essential changes proposed for reclassification of personality disorders in ICD-11 (Tyrer et al., 2011)

1. Primary classification into four or five levels of personality pathology based on severity alone
2. Identification of sub threshold level of personality difficulty (coded separately under Z-codes)
3. Secondary classification of five domains of personality disturbance: asocial/schizoid, dissocial/antisocial, obsessional/anankastic, anxious/dependent, and emotionally unstable
4. Monothetic instead of polythetic criteria necessary for inclusion
5. Simple diagnostic formulation with persistent interpersonal dysfunction at its core

Appendix 4

Bipolar affective disorder or borderline personality disorder? An exploration of patient and clinician experience

INTERVIEW GUIDE

(Version 1. 22/02/11)

Overview

The aim of this study is to gain a better understanding of how clinicians distinguish between bipolar disorder and borderline personality disorder, and to gain an insight into how this process is experienced by patients and their carers.

We will conduct semi-structured interviews of both groups ('focus groups') and individuals. These methods of data gathering will be used flexibly, depending on the development of research questions through the study. We will interview patients, and also some carers and some doctors. When we interview carers and doctors, these will ideally represent 'dyads' or 'triads', in that they will be the carer and doctor of a patient that we will also interview. This offers the potential for particularly information-rich, synergistic data gathering and development of understanding.

Individual doctor interviews

Clinician interviews will be held at the clinician's place of work. They will be of duration 30 to 45 minutes. This may incorporate review of the patients' notes to inform the discussion, with, of course, the permission of the patient.

Focus of interviews

Data gathering will focus on how clinicians distinguish between bipolar disorder and borderline personality disorder, the factors that they believe inform this distinction, and the experience of patients and their carers of this process.

Approach of interviewer(s) during interviews

Interviewer (and co-interviewer) will encourage the individual (or group) to clarify comments or to expand on them when necessary.

They will present themselves in the role of neutral observers who are particularly interested in the phenomenon under study.

Interviewers / researchers will be aware of their own preconceptions, arising both before the study began, and as a result of interviews and perusal of participant data.

DOCTOR PARTICIPANT INTERVIEW

How does the doctor distinguish the diagnosis?

What factors do they take into account and how are those weighed up

How do they experience conducting a diagnostic assessment of this nature

What are the particular challenges, their causes, and their solutions

Their views on how the process might be experienced by patients

- **Drawing interview to a close, summary and any other thoughts**

Then, the interviewer will provide a brief summary of the participant's comments, based on the brief handwritten notes. The participant will be asked whether there is anything that has been missed out.

- *So it sounds like you are saying that.... Your experiences seem to have been...*
- *Does that sound right?*
- *Anything else you would like to clarify?*
- *Or to add?*

Finally, the interview will be concluded; thank you etc; travel claim form if necessary.

Appendix 5



Understanding the assessment and diagnosis of Bipolar Disorder and Borderline Personality Disorder

We are interested in understanding your views on the assessment and diagnosis of patients with Bipolar Disorder and Borderline Personality Disorder.

This survey takes about 5 minutes to complete.

Your participation is entirely voluntary, and your responses will be strictly confidential.

Funded by the NHS

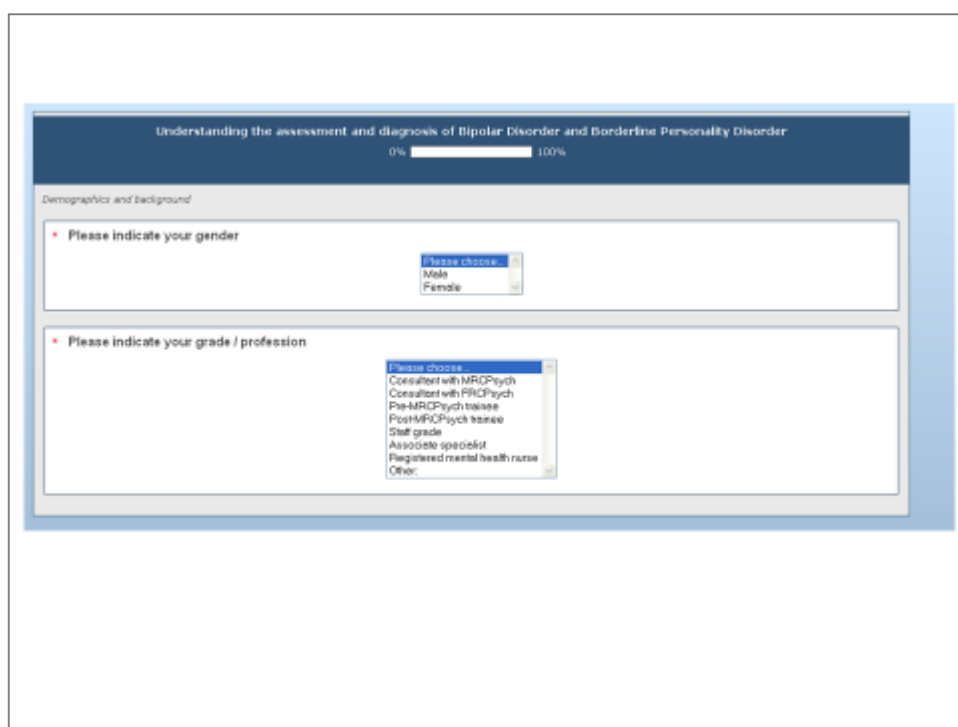
This study has been approved by NRES Committee South Central Oxford A, 11/H0604/8

Questions? Contact:
understanding-diagnosis@psych.ox.ac.uk

There are 23 questions in this survey.

[Load unfinished survey](#) [Next >>](#) [Exit and clear survey](#)

This survey is currently not active. You will not be able to save your responses.



Understanding the assessment and diagnosis of Bipolar Disorder and Borderline Personality Disorder

0% 100%

Demographics and background

• Please indicate your gender

[Please choose...](#)
Male
Female

• Please indicate your grade / profession

[Please choose...](#)
Consultant with MRCPsych
Consultant with FRCPsych
Pre-MRCPsych trainee
Post-MRCPsych trainee
Staff grade
Associate specialist
Registered mental health nurse
Other

Understanding the assessment and diagnosis of Bipolar Disorder and Borderline Personality Disorder

0% 100%

Your assessments of Bipolar Disorder and Borderline Personality Disorder

* What proportion of your caseload has a primary diagnosis of:

	<5%	5%-25%	25%-50%	>50%
...Bipolar Disorder?	☐	☐	☐	☐
...Borderline Personality Disorder?	☐	☐	☐	☐

* In what proportion of your assessments are Bipolar Disorder and Borderline Personality Disorder likely differential diagnoses?

	<5%	5%-25%	25%-50%	>50%
	☐	☐	☐	☐

Understanding the assessment and diagnosis of Bipolar Disorder and Borderline Personality Disorder

0% 100%

Confidence and Disagreement

* How confident do you feel in discriminating Bipolar Disorder and Borderline Personality Disorder?

	Not at all confident	Somewhat confident	Confident	Very confident	Extremely confident
	☐	☐	☐	☐	☐

* How often do you encounter patients with Bipolar or Borderline Personality Disorder where there has been disagreement between professionals about the diagnosis?

	Never	Rarely	Occasionally	Fairly frequently	Frequently
	☐	☐	☐	☐	☐

* In your experience, what are the TWO most common reasons for this disagreement?
Please select between 2 and 3 answers

- ☐ Inconsistent history
- ☐ Clinician background / bias
- ☐ Patients presenting in crisis
- ☐ Validity of 'soft' bipolar diagnoses
- ☐ Reliance on previous diagnoses

Other:

Understanding the assessment and diagnosis of Bipolar Disorder and Borderline Personality Disorder

0% 100%

Factors associated with BD

In your opinion, to what extent are the following features indicative of BIPOLAR DISORDER?

	Not at all	A little	Moderately	Strongly	Very strongly
Racing thoughts	☐	☐	☐	☐	☐
Onset during adolescence	☐	☐	☐	☐	☐
Identity disturbance	☐	☐	☐	☐	☐
Inflated self-esteem	☐	☐	☐	☐	☐
Drug / alcohol misuse	☐	☐	☐	☐	☐
Persistent low mood	☐	☐	☐	☐	☐
Erratic or risky behaviour	☐	☐	☐	☐	☐
Fear of abandonment	☐	☐	☐	☐	☐
Hostility	☐	☐	☐	☐	☐
Paranoid ideation	☐	☐	☐	☐	☐
Unstable interpersonal relationships	☐	☐	☐	☐	☐
Suicidal behaviour	☐	☐	☐	☐	☐
Family history of the disorder	☐	☐	☐	☐	☐
Elated mood	☐	☐	☐	☐	☐
Mood instability	☐	☐	☐	☐	☐
More talkative than usual	☐	☐	☐	☐	☐
Irritability	☐	☐	☐	☐	☐
Agitation	☐	☐	☐	☐	☐
Distractibility	☐	☐	☐	☐	☐
Early life trauma	☐	☐	☐	☐	☐
Repeated help-seeking behaviour	☐	☐	☐	☐	☐
Impulsivity	☐	☐	☐	☐	☐
Decreased need for sleep	☐	☐	☐	☐	☐
Non-suicidal self-harm	☐	☐	☐	☐	☐

Understanding the assessment and diagnosis of Bipolar Disorder and Borderline Personality Disorder

0% 100%

Factors associated with BPD

In your opinion, to what extent are the following features indicative of BORDERLINE PERSONALITY DISORDER?

	Not at all	A little	Moderately	Strongly	Very strongly
Racing thoughts	☒	☐	☐	☐	☐
Onset during adolescence	☒	☐	☐	☐	☐
Identity disturbance	☒	☐	☐	☐	☐
Inflated self-esteem	☒	☐	☐	☐	☐
Drug / alcohol misuse	☒	☐	☐	☐	☐
Persistent low mood	☒	☐	☐	☐	☐
Erratic or risky behaviour	☒	☐	☐	☐	☐
Fear of abandonment	☒	☐	☐	☐	☐
Hostility	☒	☐	☐	☐	☐
Paranoid ideation	☒	☐	☐	☐	☐
Unstable interpersonal relationships	☒	☐	☐	☐	☐
Suicidal behaviour	☒	☐	☐	☐	☐
Family history of the disorder	☒	☐	☐	☐	☐
Elated mood	☒	☐	☐	☐	☐
Mood instability	☒	☐	☐	☐	☐
More talkative than usual	☒	☐	☐	☐	☐
Irritability	☒	☐	☐	☐	☐
Agitation	☒	☐	☐	☐	☐
Distractibility	☒	☐	☐	☐	☐
Early life trauma	☒	☐	☐	☐	☐
Repeated help-seeking behaviour	☒	☐	☐	☐	☐
Impulsivity	☒	☐	☐	☐	☐
Decreased need for sleep	☒	☐	☐	☐	☐
Non-suicidal self-harm	☒	☐	☐	☐	☐

Understanding the assessment and diagnosis of Bipolar Disorder and Borderline Personality Disorder

0% 100%

Diagnostic Criteria

• To what extent do you agree with the following statements?

	Strongly disagree	Disagree	Neutral	Agree	Strongly agree
Diagnostic criteria fit with my observations of patients with Bipolar Disorder.	☐	☐	☐	☐	☐
Diagnostic criteria fit with my observations of patients with Borderline Personality Disorder.	☐	☐	☐	☐	☐
Diagnostic criteria are useful to me in discriminating between Bipolar Disorder and Borderline Personality Disorder.	☐	☐	☐	☐	☐
Rather than diagnostic criteria, I prefer to use an impressionistic or vignette approach to the diagnosis of Bipolar Disorder.	☐	☐	☐	☐	☐
Rather than diagnostic criteria, I prefer to use an impressionistic or vignette approach to the diagnosis of Borderline Personality Disorder.	☐	☐	☐	☐	☐
The diagnosis of Bipolar Disorder should involve categorization on the basis of severity.	☐	☐	☐	☐	☐
The diagnosis of Borderline Personality Disorder should involve categorization on the basis of severity.	☐	☐	☐	☐	☐

Understanding the assessment and diagnosis of Bipolar Disorder and Borderline Personality Disorder

0% 100%

Services

• Do you have access to specialized services for:

	Yes	No	Uncertain
...Bipolar Disorder?	☐	☐	☐
...Borderline Personality Disorder?	☐	☐	☐

• Does access to specialized services influence whether you make a diagnosis of Bipolar Disorder or Borderline Personality Disorder?

	Not at all	A little	Moderately	Substantially	Greatly
	☐	☐	☐	☐	☐

If you would like to comment on service provision for these patient groups, please do so in the space below (which will expand to fit your answer)

Understanding the assessment and diagnosis of Bipolar Disorder and Borderline Personality Disorder

0% ☐ 100%

Final questions

• How often do you seek third party information (e.g. from family or friends) when assessing someone with:

	Almost never / Never	Occasionally	~Half the time	Most of the time	Almost always / Always
...probable Bipolar Disorder?	☐	☐	☐	☐	☐
...probable Borderline Personality Disorder?	☐	☐	☐	☐	☐

If you would like to comment on the involvement of third parties in assessment and diagnosis of these patient groups, please do so in the space below

•

	Never	Rarely	Occasionally	Fairly frequently	Very frequently
In patients with Bipolar Disorder, how often do you give a diagnosis of comorbid Borderline Personality Disorder?	☐	☐	☐	☐	☐

•

	Definitely not	Unlikely	Neutral	Probably	Definitely
In your opinion, are Bipolar Disorder and Borderline Personality Disorder part of the same illness spectrum?	☐	☐	☐	☐	☐

Thank you for participating in this research

Funded by the NHS

Questions? Comments?

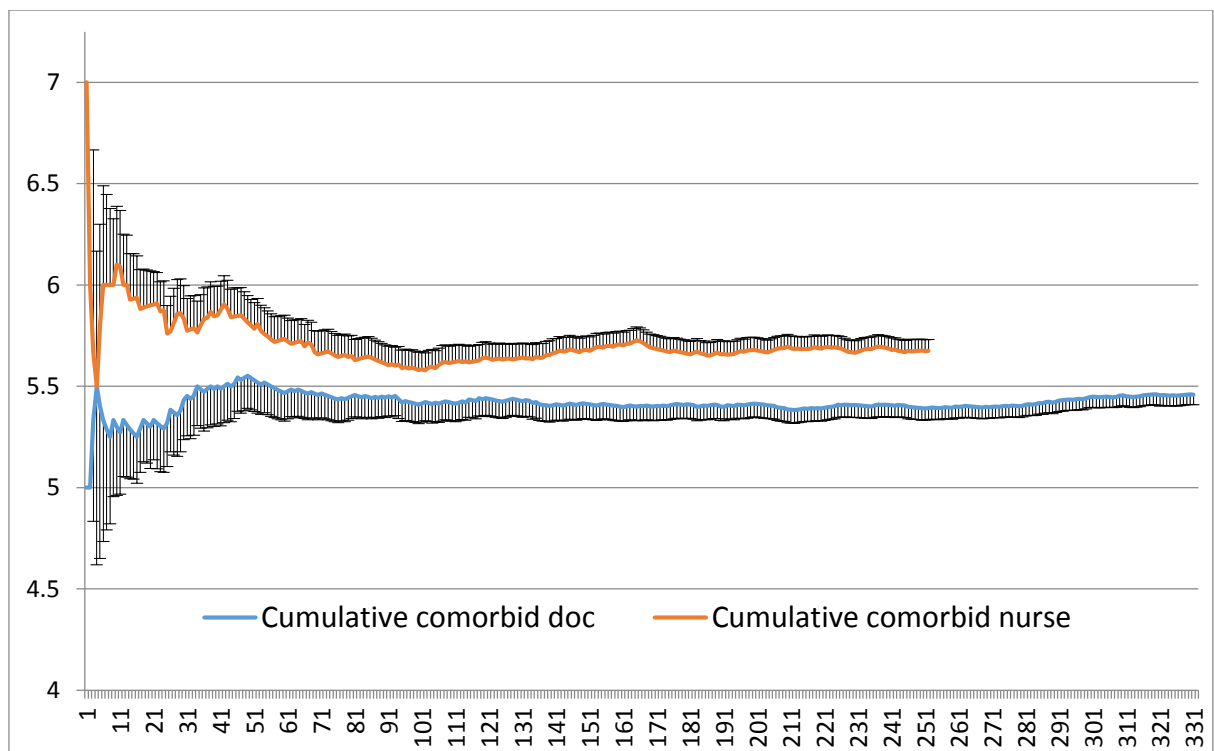
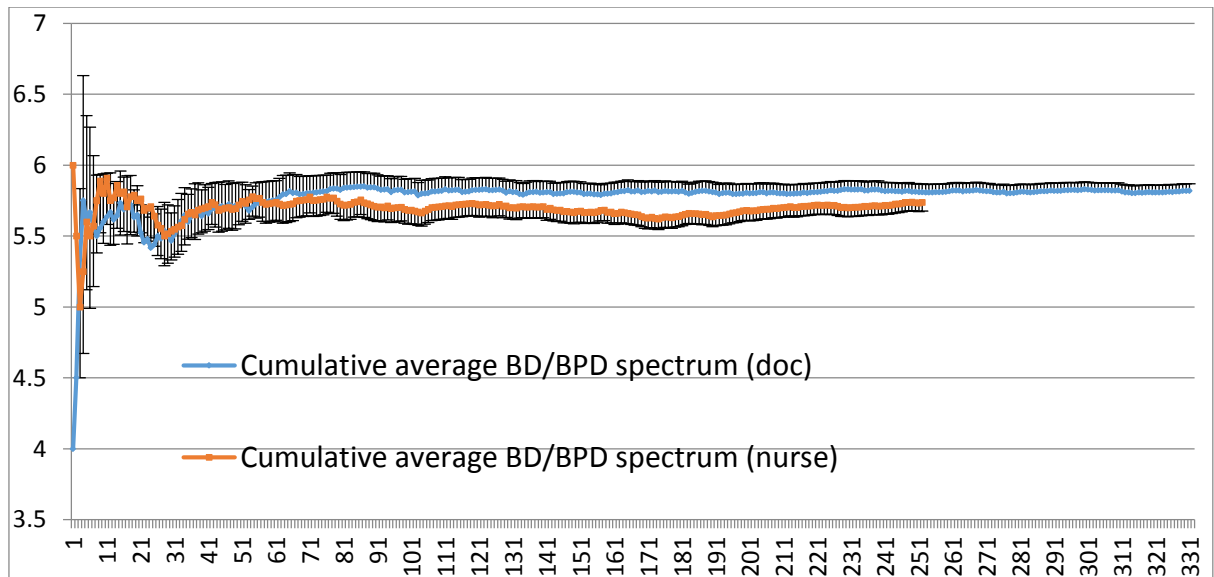
Contact: understanding-diagnosis@psych.ox.ac.uk

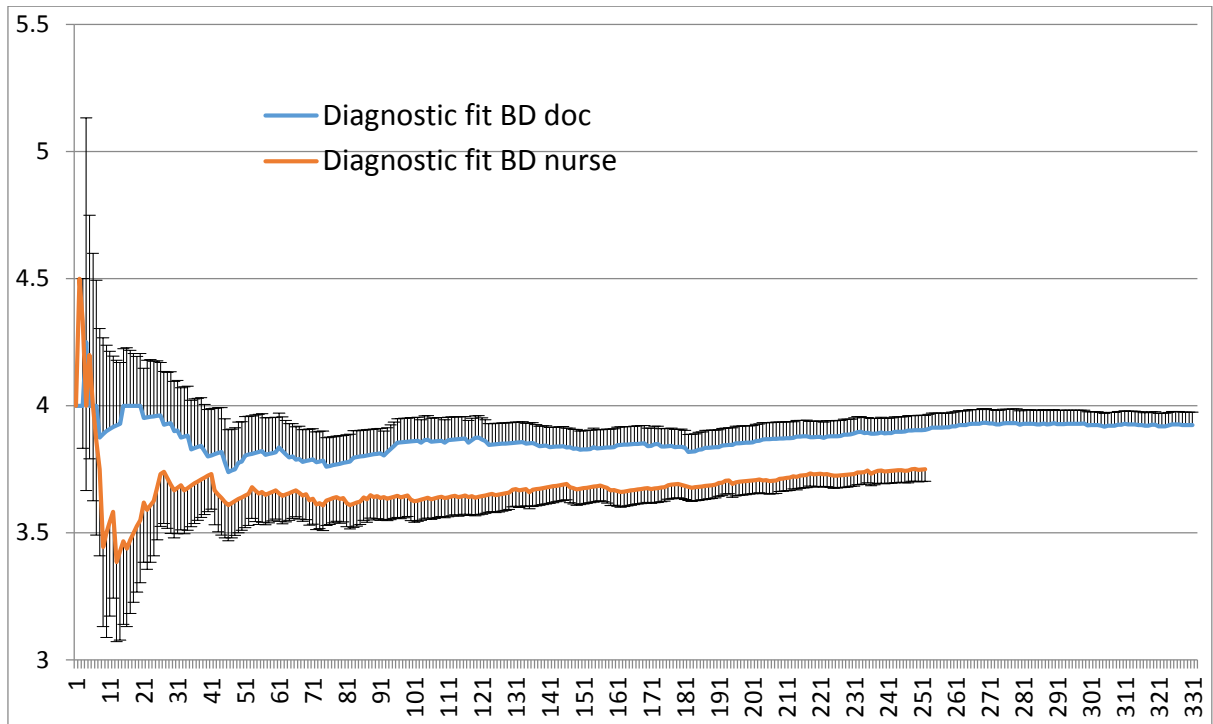
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Your survey responses have not been recorded. This survey is not yet active.

Appendix 6

Examples of the convergence of responses to the online questionnaire.





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