Explicit (self-report) measures of personality in euthymic bipolar-1 patients

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Introduction

Simple logic would suggest that there should be some endophynotype for bipolar disorder. Genetic factors account for at least half of the causal variance in bipolar disorder, and it is clear that these genes act via effects on brain structure and chemistry. Endophenotypes for bipolar disorder could be trait markers, eg of brain structure on MRI scans or in lymphocyte biochemistry (Shamir et al., 1998; Belmaker et al., 2002) but they could also be specific variations in personality or cognition (Belmaker, 2001). Other avenues explored have included emotional processing (see Mercer and Becerra, 2013 for a recent review) and the physiological correlates of emotion regulation, using fMRI technology (see review by Townsend and Altshuler, 2012). Social cognition and theory of mind have also been explored (review by Sarame et al., 2012). Our group has also conducted quantitative analyses of responses to a projective psychological test (the Rorschach Inkblot test) (Last et al., 1989; Osher et al., 2000; Osher and Bersudsky, 2007), and found thought disorder to be a possible endophenotype for bipolar disorder.

Many studies have looked at neuropsychological function (see meta-analysis by Bora et al., 2009a; see also excellent systematic review by Balanza-Martinez et al., 2008, and update by Raust et al., 2014). While some degree of cognitive impairment is generally accepted, particularly in the areas of executive function and some forms of memory, cognitive function in bipolar disorder overlaps highly with that in controls. The deficits also considerably overlap those observed in schizophrenia (Bora et al., 2009b), mild cognitive impairment (Osher et al., 2011) or even disorders such as OCD (Abramovitch et al., 2014). Thus cognitive impairment is not likely to be a useful marker for bipolar disorder.

Kraepelin conceptualized bipolar disorder as an episodic illness with recovery between episodes [to baseline personality] (Goodwin and Jamison, 2007, p.101). Goodwin and Jameson (2007) note the many methodological issues which complicate the study of bipolar personality, including the problem of “trait and state” and diagnostic and illness heterogeneity; they note also that most early studies were characterized by deficient methodologies, measurements, and design, including inappropriate control groups. They conclude that “Contemporary research generally dispels the idea that the personalities of bipolar patients are fundamentally different from those of people without mood disorders” (p. 352).

Many recent studies have emphasized the high frequency of co-morbid personality disorder in BP, including borderline, narcissistic, and obsessive-compulsive personality disorders. A recent meta-analysis by Friborg et al. (2014) concludes that approximately 40% of bipolar patients have at least one diagnosable personality disorder. Approximately one third of bipolar patients were seen to have a personality disorder from Cluster B (anti-social, borderline, histrionic, narcissistic); about one quarter were seen to have a personality disorder from Cluster C (avoidant, dependent, or ocd personality disorders, plus personality disorder NOS). Slightly more than 10% had personality disorders from Cluster A (paranoid, schizoid, schizotypal) (Friborg et al., 2014). Specifically, obsessive-compulsive personality disorder was diagnosed in 18% of bipolar patients; borderline personality disorder in 16 %, and dependent personality disorder in 13%. Approximately 12% showed avoidant personality disorder, 11% were diagnosed with paranoid personality disorder , 10% displayed histrionic personality disorder, and all other personality disorders were at or below 6% (Friborg et al., 2014). These co-morbid conditions suggest a general vulnerability but have not coalesced into a specific endophenotypical personality that could assist in pointing to a underlying neurobiological abnormality.

Other conditions which are frequently co-morbid with bipolar disorder include substance use disorders (Martins and Gorelick, 2011) and anxiety disorders (Vazquez et al., 2014). According to the results of the Epidemiological Catchment Area study published in 1990 (Regier et al.,1990) 60 % of people in the United States with bipolar 1 disorder had a lifetime diagnosis of some substance use disorder: 46% of US bipolar patients had an alcohol use disorder and 40% had a diagnosis of drug abuse or drug dependence (totaling more than 60% due to overlap of drug and alcohol use). Similarly, results from the 2000 -2002 [United States] National Epidemiological Survey on Alcohol and Related Conditions showed that *even after adjusting* for age, race or ethnicity, sex, education, income, marital status, urbanicity and geographic location – persons with bipolar 1 disorder were ten times more likely to be dependent on illicit drugs (Compton et al., 2007). Regarding anxiety disorders, people with bipolar 1 disorder showed a pooled risk of 48% (95 % CI 43-50) over 13 studies for any co-occurring anxiety disorder (Vazquez et al., 2014). Examples of prevalence rates for specific anxiety disorders included phobias (28.5%), panic (21.7%), GAD (20.3%) and PTSD (20.2%) (Vazquez et al., 2014), although the authors note that these rates may be inflated due to overlapping symptoms of anxiety and mood disorders.

 Self report measures of personality such as the TCI and NEO (described below) are widely studied in normal populations and the factors have been extracted empirically via various types of factor analysis. They have been validated in numerous cultures, and heritability of the scales has been replicably estimated at around 50%, similar to the heritability of major mental illnesses. Thus it seemed reasonable to study these self report scales in euthymic BP. We reported association of one scale, novelty seeking, to a specific dopamine receptor polymorphism (Ebstein et al.,1996). Early papers from our group found decreased persistence on the TPQ in BP disorder (Osher et al., 1996; Osher et al 1999) but this finding has generally not been replicated.

Bagby and Ryder (2000) summarized the work up to that point by noting that the related personality traits of high neuroticism and harm avoidance seem to be associated with bipolar disorder as well as with unipolar depression, whereas higher novelty seeking may be associated only with bipolar patients. In Cloniger’s model, high Novelty Seeking (together with low Harm Avoidance) is associated with impulsivity (Congdon and Canli, 2008); in Costa & MacCrea’s model, Impulsiveness is a subscale of Neuroticism [N5] but is also understood to reflect low Conscientiousness (Congdon and Canli, 2008). Therefore it is not surprising that several recent studies suggest that impulsiveness per se is significantly elevated in euthymic bipolar patients (Newman and Meyer, 2014). As these parameters are all very sensitive to affective state, it is critical to examine the literature that pertains specifically to euthymic patients in order to evaluate the extent to which this signifies underlying personality (trait), and not primarily clinical status (state).

Several important studies have been published since the Bagby and Ryder (2000) review. We restrict our current review to empirical studies which employed both adequate samples of ***euthymic*** (to minimize the state/trait dilemma) **bipolar I** patients as well as **healthy comparison subjects**. We will not include studies with mixed samples of bipolar I and bipolar II patients, since it is not possible to conclude if any deviation from normal results from the bipolar I or the bipolar II sample, and since bipolar II samples may include many misdiagnosed patients with borderline personality disorder.

This paper is restricted to explicit measures of personality – that is, self report questionnaires; in a future paper we hope to explore implicit (indirectly assessed, behavioral) measures as well. Many studies using explicit measures of personality used either the Temperament and Character Inventory (TCI) based on Cloninger’s psychobiological theory of temperament and character (Cloninger et al., 1993), or the Revised NEO Personality Inventory based on the five-factor model of Costa & McCrae (1992). In addition, we found a set of four studies meeting our criteria which related to an additional facet of personality, impulsivity, as measured by the Barratt Impulsiveness Scale (BIS-11)(Patton et al., 1995).

**TCI studies**

Based on Cloninger’s psychobiological theory (1993), the 240-item TCI measures four dimensions of temperament and three dimensions of ‘character’. The temperament dimensions are Novelty Seeking (NS), Harm Avoidance (HA), Reward Dependence (RD), and Persistence (P). The latter was originally a subscale of Reward Dependence but was later shown to be an independent factor. The character dimensions consist of Self-Directedness, Cooperativeness, and Self-Transcendence. Each dimensional score is a composite of several subscales (except for Persistence) which will not be discussed here individually for the sake of clarity.

We found two studies (Engstrom et al., 2004; Almeida et al., 2011) which fully met our criteria. We found one other study (Harley et al., 2011) which included euthymic BP I subjects, but used a slightly different version of the TCI, and used unaffected relatives as the healthy comparators. Table 1 summarizes the findings (presented as means with SD in parenthesis).

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|  | Engstrom 2004 | Almeida 2011 | Harleya2011 |
| TCI Scale | BPN=75 | HCN=100 | BPN=67 | HCN=67 | BPN=60 | HCN=87 |
| NS | 17.8 (5.0) | 18.1 (5.3) | 20.13\*\*(5.99) | 17.14(3.66) | 18.78(6.66) | 17.37(5.73) |
| HA | 16.1 (7.1) | 14.5 (6.2) | 20.15\*\* (7.09)  | 9.26 (4.10) | 18.78\*\* (8.57) | 11.91 (6.38) |
| RD | 13.8\* (3.4) | 15.1 (3.6) | 14.64 (3.98) | 15.91 (2.86) | 23.37 (6.40) | 22.43 (5.74) |
| P | 3.6 (1.9) | 3.7 (1.7) | 4.69 (1.82) | 5.06 (1.44) | 22.75 (10.50) | 26.06 (8.65) |
| SD | 31.7 (6.7) | 33.1 (6.4) | 27.70\*\* (8.08) | 37.67 (4.13) | 31.13\*\* (8.51) | 37.34 (6.11) |
| COP | 32.3\* (5.0) | 34.2 (4.2) | 30.21\*\* (5.82) | 33.90 (2.92) | 33.88 (6.89) | 35.57 (5.92) |
| ST | 12.0 (6.2) | 12.8 (5.9) | 18.69\*\* (5.73) | 12.74 (5.15) | 22.43\*\* (12.30) | 15.39 (10.99) |

\*p< 0.05

\*\* p< 0.01

Table 1. Summary of studies comparing euthymic bipolar I patients and healthy controls using Cloninger’s Temperament & Character Inventory. Temperament dimensions are Novelty Seeking (NS), Harm Avoidance (HA), Reward Dependence (RD), and Persistence (P). Character dimensions consist of Self-Directedness (SD), Cooperativeness (COP), and Self-Transcendence (ST).

a Healthy controls were non-affected relatives, and the instrument used was the TCI-R, a later version of the TCI with expanded Reward Dependence and Persistence scales

**NEO-PI-R studies**

Based on the five factor model of Costa and McCrae (1992), the Revised NEO Personality Inventory (NEO-PI-R) is a 240-item self report questionnaire which provides summary scores for the “five factors” of personality: Neuroticism (N), Extraversion (E), Openness to experience (E), Agreeableness (A) and Conscienciousness (C).

We were not able to find a single study using the NEO-PI-R which directly compared a euthymic sample of BP I patients to a group of healthy controls. We found one study (Kim et al., 2012) which compared the scores of Korean euthymic BP I patients to the scores of a Korean normative sample which had been published 20 years earlier. Results are summarized in Table 2.

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| --- | --- |
|  | Kim et al., 2012 |
| NEO Scale | BP IN=85 | Normative Samplea N=692 |
| Neuroticism | 97.8(26) | 93.0(21) |
| Extraversion | 107.5(24) | 108.4(18) |
| Openness | 103.0\*(14) | 108.5(17) |
| Agreeableness | 116.0\*(17) | 120.5(15) |
| Conscientiousness | 113.6\*(24) | 121.6(21) |

\*small effect size (0.50>d>0.2)

Table 2. Summary of study comparing euthymic bipolar I patients and normative sample data using the NEO-PI-R.

aAhn et al., 1997

**Impulsivity**

A comprehensive recent review of impulsivity in euthymic bipolar patients (Newman and Meyer, 2014) looked separately at self report and behavioral measures. They concluded that “…studies using self-report measures suggest impulsivity is a trait of those who experience BD rather than only ‘state’ related” (p.13/16). All ten studies in the self-report category used versions of the Barratt Impulsiveness Scale (Barrett, 1959). Of those, four reported samples composed of BP I patients exclusively (Stakowski et al., 2010; Lombardo et al., 2012; Ekinci et al., 2011) or almost exclusively (90%: Lewis et al., 2009).

The BIS-11 (Patton et al., 1995), the version currently in widest use, consists of 30 self-statements which are rated by the respondent on a scale of 1 (rarely/never) to 4 (almost always/always). Total impulsivity as measured by the BIS-11 has been found to be highly heritable (Seroczynski et al., 1999), and has even been associated with specific serotonergic and dopaminergic polymorphisms (Varga et al., 2011). In addition to the total score, three second-order subscales have been derived and are often reported: Attentional, Motor, and Non-planning. Total scores between 52 and 71 are considered “within normal limits”; scores of 72 and above would be classified as “highly impulsive” (Stanford et al., 2009). Results for euthymic BP I patients and healthy controls are summarized in Table 3. While one study (Lewis) did not find differences in the total score, the other three studies found the euthymic BP group to score significantly higher than healthy controls on total impulsivity.

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| --- | --- | --- | --- | --- |
|  | Lewisa2009 | Strakowski2010 | Ekinci2011 | Lombardo2012 |
| BIS-11Scale | BPN=36 | HCN=30 | BPN=28 | HCN=35 | BPN=71 | HCN=50 | BPN=54 | HCN=49 |
| TOTAL | 58.7(8) | 60.8(10) | 61\*\*(11) | 51(8) | 74.3\*\*(7.8) | 50.3(3) | 72.9\*(12) | 52.4(9) |
| Attentional | 14.6(3) | 14.5(3) | 14(4) | 12(2) | 21.2\*\*(4) | 18.3(2) | 18.7\*(4) | 12.3(3) |
| Motor | 20.2(3) | 22.8(4) | 23\*\*(5) | 19(3) | 24.9\*\*(3) | 17.0(2) | 26.1\*(5) | 19.8(3) |
| Non-planning | 23.9(4) | 23.5(5) | 24\*(5) | 20(4) | 28.1\*\*(3) | 21.4(3) | 28.0\*(5) | 20.3(4) |

\*p< 0.05 \*\*p<0.01

Table 3. Summary of studies comparing euthymic bipolar I patients and healthy controls using the Barratt Impulsiveness Scale (BIS-11)

aBipolar I constituted 90% of this sample; others BP II or NOS

**Discussion**

Clearly, there is no single dimension of ‘personality’ reviewed above which would qualify as a psychological marker for bipolar disorder. Earlier findings as reviewed by Bagby and Ryder, of higher Novelty Seeking, were not replicated in these studies, perhaps due to our emphasis on highly euthymic patients. While there are significant differences between group means in many instances, these differences are often not replicated across studies (for example Self-directedness and Self- transcendence in the NEO). Even more to the point, even large group differences which are consistently replicated – for example, increased Harm Avoidance scores – reveal a large overlap in scores between the bipolar and the healthy control groups. Such a large overlap would certainly preclude the use of HA scores as a diagnostic tool, or as a tool which could reliably identify at-risk individuals. As has been discussed in relation to evidence-based psychopharmacology (Belmaker et al., 2012), there is a huge gap between group differences and discriminations which must be made at the individual level.

This is not to say that there is no indication that some of these traits could prove to be useful endophenotypes. As an example, Almeida et al. (2011) noted that the non-affected relatives of the bipolar probands scored, as a group, levels of Harm Avoidance and of Self-transcendence which fell between the bipolar and the healthy (unrelated) control group.

Of the personality traits considered, the most promising candidate for marker or endophenotype would seem to be “impulsivity” as measured by the BIS-II. Three out of four studies found euthymic bipolar I patients scoring consistently higher on all three subscales, and strikingly higher on the BIS-II total score, as compared to healthy controls. The Lombardo et al. (2012) study included a comparison group of unaffected siblings and found them to show intermediate scores, which were still significantly higher than the healthy control group, on BAS-II total and two of the three subscales. The Strakowski et al. (2010) paper reinforces the idea that higher impulsivity as measured by the BIS-II is in fact a trait, and not state dependent: while performance on three behavioral measures of impulsivity normalized as patients moved from manic or mixed conditions to euthymia, the BAS-II scores remained elevated in euthymia and even when patients developed depression. Similarly, Swann et al. (2003) found that total BIS scores were identical in euthymic (N=22) and manic (N=12) bipolar patients (not known if euthymic patients were BP I, BP II, or a mixed group). A recent meta-analysis (Saddichha and Schuetz, 2014) found strong evidence that impulsivity as measured by the BIS II is significantly higher in bipolar patients as compared to controls; this review included studies of adolescent as well as adult patients, patients who were manic or depressed as well as in varying states of euthymia, and studies including a combination of BP I and BP II patients. Still, it should be noted that the fourth study included in our review (Lewis et al., 2009) found no differences between euthymic bipolar patients and healthy controls, but did note “a significant incremental increase across subscale scores between remitted and symptomatic [bipolar patient] groups” (p. 466). Additional studies with strictly euthymic patients would be helpful to settle this point.

An additional caveat is required: certain traits may characterize euthymic bipolar patients (sensitivity), but may not be restricted to bipolar disorder (specificity). Higher Harm Avoidance, for example, was found in the papers we reviewed, as was true in the earlier review by Bagby and Ryder (2000), but was also found in unipolar depressive patients as noted by Bagby and Ryder and also in euthymic unipolar depressives in well designed newer studies (Smith et al., 2005; Ekinci et al., 2012). Higher impulsivity as measured with the BIS-11 has also been reported in young euthymic major depressive disorder patients (Ekinci et al., 2011), although 14 of the 60 MD patients reported a previous psychotic mood episode – which raises at least the suspicion that some of these subjects may in fact, over time, be revealed to be bipolar rather than unipolar patients.

It is the stable ‘baseline’ which we refer to as our patients’ personalities. Many traits appear and disappear *in patients* over the course of an affective episode. We do not consider these transient qualities to be part of the the patient’s personality. Only studies involving patients who are assessed *when as fully euthymic as possible* can contribute meaningful information to the question of whether or not there is such a thing as a “bipolar personality” or “bipolar temperament”. Clinical mood states affect self-report of personality (see for example Barnett et al., 2011 regarding the NEO; Nery et al., 2009 regarding the TCI).

 Akiskal, on the other hand, is a proponent of testing for "temperament" even when patients are acutely ill: "Our intention was to find out about the patients' temperaments whenever they presented clinically - which of course is when it would be most useful to the clinician to know something about the patients' temperament"  (2005, p. 8). This in spite of the fact that the great many of the items in the TEMPS are clearly going to be strongly impacted by depressive or manic state:  "My feelings are easily hurt by criticism or rejection", "I often feel tired for no reason", "I feel all emotions intensely" "Life is a feast which I enjoy to the fullest", "I have great confidence in myself", "I can accomplish many tasks without even getting tired", "I have abilities and expertise in many areas", "I feel very uneasy meeting new people", and so on. Akiskal contends that "it is unlikely" that the measured temperament traits are state dependent - because subjects are routinely instructed to “circle an item on the TEMPS-A in the affirmative only if it characterized them for much of their lives since at least early adulthood".   Our clinical experience is more consistent with the approach of Aaron Beck, in that affectively unstable patients have perceptions of the self that are distorted not only as relates to the present, but also to the past and future. We were unable to find a study utilizing the TEMPS-A in a reasonably large, well defined BP I group that met the usual criteria for euthymia - the closest was a study where the *average* mood scale scores of the patient group were approximately what is usually used as cut-off points for defining euthymia (Mahon et al., 2013). For this reason, we have not included studies utilizing the TEMPS-A in this review.

Certain specific traits, such as higher impulsivity, may be more common in euthymic bipolar patients than in healthy controls, and may even prove useful in decoding the complex genetic architecture underlying the disorder (eg Jimenez et al., 2014). Impulsivity may also have clinical prognostic implications: there is some evidence that impulsivity is associated with overall functional impairment in euthymic bipolar patients, even after accounting for depressive symptoms and number of hospitalizations (Jimenez et al., 2012). There is also some evidence that higher BIS-II scores, even while bipolar I patients are euthymic, are associated with lifetime suicidal behavior (Nery-Fernandes et al., 2012). Other characteristics uncommonly common in bipolar patients, such as certain personality disorders, anxiety disorders, and increased susceptibility to substance use disorders may also hold clues to the heritability and genetic architecture of bipolar disorder: there is evidence of high heritability for avoidant and dependent personality disorders (Gjerde et al., 2012) as well as for one highly heritable general borderline personality disorder factor (Reichborn-Kjennerud et al., 2013). For any of the traits discussed above, however, including impulsivity, there are many bipolar patients who do not display them as expected, as well as many healthy individuals who do express them. We conclude, therefore, that while certain personality traits may be common in euthymic bipolar patients - most notably impulsiveness –extant research in explicit measures has not, as of yet, identified a clear personality-related endophenotype for this disorder.