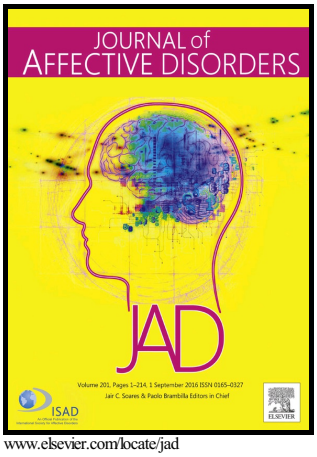

www.elsevier.com/locate/jad

Increased reward-oriented impulsivity in older bipolar patients: a preliminary study

Isabelle E. Bauer, Breno Satler Diniz, Thomas D. Meyer, Antonio Lucio Teixeira, Marsal Sanches, Danielle Spiker, Giovana Zunta-Soares, Jair C. Soares

PII: S0165-0327(17)30861-3
DOI: http://dx.doi.org/10.1016/j.jad.2017.08.067
Reference: JAD9186

To appear in: *Journal of Affective Disorders*

Received date: 28 April 2017
Revised date: 2 August 2017
Accepted date: 20 August 2017

Cite this article as: Isabelle E. Bauer, Breno Satler Diniz, Thomas D. Meyer, Antonio Lucio Teixeira, Marsal Sanches, Danielle Spiker, Giovana Zunta-Soares and Jair C. Soares, Increased reward-oriented impulsivity in older bipolar patients: a preliminary study, *Journal of Affective Disorders,* http://dx.doi.org/10.1016/j.jad.2017.08.067

Title: Increased reward-oriented impulsivity in older bipolar patients: a preliminary study

Running title: impulsivity in older bipolar patients

Keywords: impulsivity, bipolar disorder, old age, cognitive control, reward

Isabelle E. Bauer[1], Breno Satler Diniz[1], Thomas D.Meyer[1], Antonio Lucio Teixeira[1], Marsal Sanches[12], Danielle Spiker[1], Giovana Zunta-Soares[1], Jair C. Soares[1]

[1]University of Texas Health Science Center at Houston, McGovern Medical School, Department of Psychiatry and Behavioral Sciences, 77054 Houston, TX, United States

[2]Archway Mental Health Services, 58502 Bismarck, ND, United States

Words

Abstract: 193

Article body: 3966

Number of figures: 1

Number of tables: 2, 2 Tables for the Supplementary material

Corresponding author

Isabelle Bauer

University of Texas Health Science Center at Houston

Department of Psychiatry and Behavioral Science

McGovern Medical School,

1941 East Road

77054 Houston, TX, USA

Email: Isabelle.E.Bauer@uth.tmc.edu

Ph: (713) 486-2624

Declaration of interest

Drs Bauer, Satler Diniz, Teixeira, Spiker, and Zunta-Soares have no conflicts of interest

Dr. Sanches has received research grants from Janssen.

Dr Soares has received grants/research support from Forrest, BMS, Merck, Stanley Medical Research Institute, NIH and has been a speaker for Pfizer and Abbott.

Role of funding source

This work was partly supported by the Stanley Medical Research Institute, the Dunn Foundation, NIH grant MH 085667 (JCS), and by the Pat Rutherford Jr. Chair in Psychiatry (UTHealth).

Contribution

MS, DS, GZS and JCS designed the study, wrote the protocol and collected the data. IB undertook the statistical analysis and wrote the first draft of the manuscript. BSD read and revised the first draft of the manuscript. TM and AT contributed to and have approved the final manuscript.

Abstract

Objective: Impulsivity is a well-established trait of bipolar disorder (BD) that persists across mood phases. It is, however, still unknown whether, in BD, impulsivity remains stable or varies in intensity over the lifespan. This cross-sectional study compared impulsive behavior in older euthymic BD patients and healthy individuals using a range of self-rating and behavioral measures of impulsivity.

Methods: 28 BD patients (56.07±4.08 years, 16 women) and 15 healthy controls (HC; 55.1±3.95 years, 6 women) were administered the Barratt Impulsivity Scale (BIS) and selected tasks of the Cambridge Neuropsychological Test Automated Batter (CANTAB) reflecting impulsivity. Multivariate analysis of variance controlled for age compared impulsivity measures across BD and HC.

Results: BD patients displayed poor decision making, risk taking, and increased delay aversion. Other measures of impulsivity such as response inhibition, sustained cognitive control, and BIS scores were, overall, comparable between BD and HC.

Conclusions: These preliminary findings suggest that, in BD, aspects of impulsivity related to reward-based decision making persist into late adulthood. Large scale, longitudinal studies are needed to evaluate the relationship of age to impulsivity over time, and explore the link between impulsivity and illness progression in elderly individuals with BD.

Objective

Mental illness affects 20% of individuals aged 55 years or older, with the most prevalent conditions including bipolar disorder (BD), depression, and anxiety (CDC., 2008). In spite of the growing body of research highlighting the link between aging, mood disorders and cognitive impairment (Almeida et al., 2016; Fung et al., 2016), chronic health issues, (Chapman et al., 2005), and earlier mortality (Mezuk and Gallo, 2013) in adults with BD, mood disorders are still under-recognized and undertreated among older individuals.

Of particular relevance in BD research is the construct of impulsivity, which is an important predictor of poor clinical outcomes (Swann et al., 2009a) and risk-taking behaviors (Chamorro et al., 2012). A large body of research has shown that BD is characterized by reduced impulse control (Ernst et al., 2004; Johnson, 2005), reflected by poor reward-related decision making (Linke et al., 2012; Nusslock et al., 2012), inefficient money management skills (Cheema et al., 2015), and self-injurious behaviors (Simon et al., 2007). Current literature has, however, focused on young adults with BD and no study has explored whether, in older adults with BD, impulsivity is increased or comparable to that of elderly individuals with no lifetime history of mental illness.

Aging affects some facets of impulsivity more than others. A study using a laboratory-based behavioral measure of impulsivity (Matching-Familiar-Figures Test) indicated that elderly healthy adults (mean age:70.6 years) were more impulsive (in the form of reduced accuracy and faster response times) than young individuals (mean age: 21.9 years) (Coyne et al., 1978). Another large sample study (n=2725) using a well-

established self-rating measure of impulsivity (Behavioral Inhibition System and Behavioral Activation System; Carver and White, 1994) found that older individuals were less impulsive on self-rating behavioral inhibition and activation scales than the younger groups (Jorm et al., 1998). It has been suggested that, while dysfunctional impulsivity (e.g. tendency to make risky decisions) generally increases over time, functional impulsivity (e.g. tendency to make quick decisions with likely personal gain) is quite stable over the lifespan (Morales-Vives and Vigil-Colet, 2012). A study examining delay discounting showed that older adults discount monetary rewards at a slower rate than younger adults, which may reflect better self-control and an increased ability to appreciate delayed rewards (Jimura et al., 2011). Indeed, whereas children favor instant rewards, older adults focus on future, greater rewards (Drobetz et al., 2012). However, decreased life expectancy may counteract this trend, as individuals realize they have less time to benefit from delayed rewards. Indeed, a study on delay of gratification in older adults aged 60 to 94 years concluded that individuals aged over 80 years were overall more impulsive than those aged 60-69 years (Forstmeier et al., 2011). These results highlight the multidimensional nature of impulsivity (Meda et al., 2009) and the need for including a variety of measures, e.g. self-rated and behavioral measures, to study this concept.

With regard to impulsivity in BD, while clinical studies use self-rated measures of impulsivity (e.g. Barratt Impulsivity Scale), neuropsychological studies (Ethridge et al., 2014; Powers et al., 2013) view impulsivity as related to poor response inhibition and test it through tasks of the Go/No-Go type (Chamberlain and Sahakian, 2007), and measures of reward sensitivity, e.g. gambling and decision making tasks (Bauer et al.,

2015; Christodoulou et al., 2006; Mason et al., 2014). It is noteworthy to mention that inhibitory control plays a critical role a number of important mental processes such as memory, attention, and affective processing (Bechara, 2005; Salgado et al., 2009). For instance, highly impulsive individuals typically struggle to inhibit prepotent responses to distracting stimuli, and make a high number of commission errors (Salgado et al., 2009). Further, the few studies on sustained attention and affective processing (Leibenluft et al., 2007; Walshaw et al., 2010) show that BD patients display impulsive, generally mood-congruent, responses to emotional stimuli, e.g. faster reaction times in response to positive *vs* negative stimuli in manic BD patients (Murphy et al., 1999; Roiser et al., 2009). It could be argued that self-rating impulsivity measures are more likely to capture trait-related aspects of impulsivity than laboratory-based tasks (Lai et al., 2011). However, there is evidence that impulsive responses to positive or negative stimuli acquired during affective episodes are independent from individuals' current mood state, and persist during the euthymic states (Linke et al., 2011). Further, a longitudinal study on cognitive changes in unipolar and bipolar patients showed that only individuals with past severe depression displayed cognitive deficits (Sarapas et al., 2012). This is in line with previous evidence that cognitive performance is not strongly affected by current mood state (Gruber et al., 2007). This may mean that, when examining behavioral measures of impulsivity, the distinction between "trait" and "state-related" impulsivity may be more blurred than previously believed. Focusing on the multidimensional construct of impulsivity may, therefore, be more informative than comparing state vs trait impulsivity.

Our previous work using laboratory-based tasks of impulsivity in adult BD patients with and without a lifetime history of substance use found a trend suggesting a relationship between a lifetime history of substance use and increased propensity to risk-taking on the Cambridge Gambling Task (Cambridge Neuropsychological Test Automated Battery - CANTAB; Bauer et al., 2015). In a separate sample of euthymic BD patients we found that the quality of decision making on the CGT was reduced in medicated adults with BD when compared to healthy controls (Wu et al., 2016). Reduced reward-related decision making may, therefore, persist in euthymic periods, regardless of the patients' medication status.

The literature linking impulsivity, aging and BD is unfortunately limited and somewhat contradictory. Two longitudinal studies showed a decline in performance on the Mini-Mental State Examination (Dhingra and Rabins, 1991), and the Dementia Rating Scale (Gildengers et al., 2009). Three studies did not find evidence of significant cognitive decline in old BD patients when compared to HC over a period of 2 to 5 years (Depp et al., 2008; Schouws et al., 2016; Schouws et al., 2012). Notably, Depp et al. (2008) reported that, in the BD sample, there was significant intra-individual cognitive variability between time points. Further, this variability did not appear to be related to baseline measures or changes in the severity of affective symptoms (Depp et al., 2008). Another study showed that elderly BD displayed a more pronounced slowing in processing speed compared to healthy elderly individuals (Lewandowski et al., 2014). Taken together these finding indicate that intra-individual variability in cognitive performance is a core feature of aging. This may be due to age-related alterations in cognitive abilities required for decision making, e.g. some individuals may be slow in

learning to associate high-value tokens and low gains. Since the majority of these studies used summary or total cognitive scores and did not report results for specific cognitive domains (e.g. attention, executive functions), the interpretation of current findings with regard to impulsivity is limited. Further, to date, “neuropsychological” aspects of impulsivity such as inhibitory control and decision making have not been examined in an older BD population.

In sum, impulsive tendencies may contribute to risky behaviors (e.g. suicide) and poor clinical outcomes in BD. Aging is characterized by cognitive changes and increased exposure to stressful physical and environmental changes. In BD, aging could, therefore, impair decision-making, and lead to an even higher risk for maladaptive behaviors. Given the potential link between aging, impulsivity, and mental health, additional work is needed to characterize the performance of elderly BD patients on various impulsivity facets. To address this issue we conducted a cross-sectional study to compare a range of behavioral and self-rating measures of impulsivity in individuals aged 50 years and above to that of elderly individuals with no lifetime history of mental illness. Our working hypothesis was that older BD patients would display increased self-rated and behavioral impulsivity compared to older healthy controls with no lifetime history of mental illness.

Methods

Sample and psychiatric assessment

The sample included 15 healthy controls (HC; M±SD: 55.1±3.95years, 6 females) and 28 adult BD patients (M±SD: 56.07±4.08 years, 16 women) (see Table 1). Participants were recruited from inpatient and outpatient clinics of the University of North Carolina at Chapel Hill (UNC)(n=21:10HC, 11BD) and the University of Texas Health Science Center at Houston (UT)(n=22: 5HC, 17BD). HC were recruited via oral presentations and flyers. Specific inclusion criteria for HC were: no current or lifetime axis I psychiatric diagnosis, no lifetime history of substance use disorder, no previous history of neurologic disorders including head injury with loss of consciousness for any period of time, pregnancy, family history of hereditary neurologic disorder, psychiatric disorder in first-degree relatives, use of any prescribed psychiatric medication in their lifetimes. Participants were excluded if they had any current serious medical problems including cardiovascular and neurological disorders. Medication was not an exclusion criterion. The diagnosis of BD among patients were ascertained by the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders Axis I (SCID I) (First et al., 2012). The SCID was administered to all participants by an independent psychiatrist or trained research assistant. The clinical interview also included the Montgomery-Åsberg Depression Rating Scale (MADRS)(Montgomery and Asberg, 1979) and the Young Mania Rating Scale (YMRS) (Young et al., 1978). All participants were administered the Full Scale IQ (WASI) (Wechsler, 1999) which is a measure of premorbid intellectual quotient (IQ). The study protocol was approved by the local Institutional Review boards at both recruitment sites and informed consent was obtained from all the participants.

Table 1 about here

Impulsivity

BIS

The Barratt Impulsivity Scale (BIS) (Patton and Stanford, 1995) is a 30-item self-report measure of impulsivity that includes three subscales: attentional impulsivity (e.g. difficulties with concentrating), motor impulsiveness (e.g. motor restlessness), and non-planning impulsiveness (e.g. self-control.) Items are coded from 1 (rarely/never) to 4 (always/almost always) and their sum provides a total score ranging from 30 to 120. Total BIS scores typically range from 30 to 120, with higher scores indicating greater impulsivity. BIS has well-established satisfactory test-retest reliability and internal consistency (Cronbach's α = .83) (Patton and Stanford, 1995).

CANTAB

Behavioral aspects of impulsivity were measured by the Affective Go/No-Go task (AGN), Cambridge Gambling Task (CGT), and the Rapid Visual Processing Task (RVP) of the computerized Cambridge Neurocognitive Test Automated Battery (CANTAB - http://www.cantab.com)(Robbins et al., 1998) This battery was chosen based on its

established sensitivity to altered cognitive functioning in psychiatric disorders (Sweeney et al., 2000). The tasks of the CANTAB included in the present study are briefly described below.

Affective Go/No-Go (AGN): in this task participants are instructed to respond to either happy (e.g. joyful, warmth, courage) or negative words (e.g. mistake, hopeless, burden), and inhibit their response to stimuli of opposite valence. Stimuli were presented in both a random (shift: negative, positive, positive, negative) and sequential way (non-shift: positive, positive, negative, negative). The outcome measures included in this manuscript are: 1. mean reaction times and number of commission errors in response to all stimuli, and 2. mean reaction times and number of commission errors to positive and negative stimuli. A high number of commission errors reflects the inability to inhibit unwanted responses to emotionally salient stimuli.

Cambridge Gambling Test (CGT) evaluates impulse control and risk-taking behavior. Primary outcome measures include 1. deliberation time prior to making a bet, 2. risk taking (mean proportion of the number of points bet on trials with a more likely outcome), 3. risk adjustment (tendency to bet a high proportion of points on trials with a more likely outcome, e.g. high score indicates decreased risk taking), 4. quality of decision making (proportion of bets on gamble trials with a more likely outcome), and 5. delay aversion (ratio score representing the ability to bet large amounts depending on the odds of winning/losing, e.g. a high score reflects the inability or unwillingness to refrain from betting).

Rapid Visual Processing (RVP) is a test of continuous performance and visual sustained attention. In this task, digits from 2 to 9 appear in a pseudo-random order on the screen. Participants are instructed to click on a press pad every time they see target sequences of digits (e.g. 2-4-6, 3-7-9). The main outcome measures of this task in relation to the concept of impulsivity are RVP A" (ability to distinguish targets from non-targets; scores range from 0 to 1 with 1 representing perfect detection), RVP B'' (tendency to respond to a target regardless of whether a target sequence is presented; scores range from 0 to 1, with 1 representing a prepotent response tendency), and mean response latency.

Statistical procedure

Statistical analyses were performed using IBM SPSS statistics (Version 21.0). Normality assumptions for continuous variables were examined. One-way ANOVAs and chi-square (χ^2) analyses were used to compare demographic and clinical differences between groups. We examined the coefficients of correlation across estimates of impulsivity and identified strong correlations(r>.5) between the number of CGT overall proportion bets and CGT Risk taking (r=.98), between AGN reaction times and between AGN commission errors (r coefficients ranged from .85 and .94 across emotional valences). The BIS total score correlated strongly with the other BIS subscores (r ranging from .52 to .57). Further, the RVP total number of hits correlated strongly with RVP A' (r=.93, p<.01). To avoid multicollinearity issues we approached our analyses in the following manner. To start with, we removed the variable "number of CGT overall

proportion bets" and RVP total number of hits from subsequent analyses and calculated the coefficients of correlation among the remaining impulsivity measures (Supplementary Table 2). To address the issue of strong correlations between BIS scores and between AGN variables we conducted four separate univariate and multivariate analyses of variance (M/ANOVA) including BIS total score (1), AGN reaction times and accuracy to all stimuli (2), AGN reaction times and accuracy to positive stimuli (3), and AGN reaction time and accuracy to negative stimuli (4). Three additional MANOVAs were conducted and included: BIS subscale scores, CGT variables (Deliberation time, Delay Aversion, Quality of Decision Making, Risk taking, Risk Adjustment), and RVP variables (RVP A', RVP B', reaction time, number of false alarms) (Table 3). Based on previous evidence suggesting that aging correlated negatively with impulsivity (e.g. Meyer and Hautzinger, 2001) and is associated with increased reaction times (Brown et al., 2012), age was entered as a covariate to all M/ANOVA analyses (Supplementary Table 1). To account for potential site differences, we planned to covary impulsivity measures found to be significantly different between HC and BD for site effects, including both site main effects and site by group interaction. Given the role of medication on cognition (Daglas et al., 2016; Sabater et al., 2016), we compared performance on significantly different impulsivity measures between medicated and unmedicated BD patients. In our previous paper (Bauer et al., 2015) illness chronicity (estimated by the number of mood episodes and hospitalizations) was not found to be predictors of impulsivity. These variables were therefore not included as covariates. All analyses were adjusted for multiple comparisons using Bonferroni

correction and statistical significance was defined as p<.05. In the results section we will quote SPSS Bonferroni adjusted p-values (Bland and Altman, 1995).

Results

Demographics

HC and BD were comparable in terms of age, gender, and IQ scores. The number of years of education and GAF scores was greater in HC than in BD (p<.01). As expected, patients with BD reported higher levels of depressive and manic symptoms (p<.001). Although not clinically significantly elevated, scores on the YMRS and MADRS suggested, on average, subthreshold levels of mania and mild depression (Table 1). The number of enrolled BD and HC individuals was comparable between study sites ($\chi^2(1)=2.93$, p=.09),and there were no significant differences in age, gender, ethnicity, years of education between study sites (p>.05).

BIS

Differences in BIS subscores between groups approached significance [Pillai's trace $F(3,35)=2.71$, p= 0.06, partial $\eta^2= 0.19$], and HC displayed marginally greater BIS attentional impulsivity scores compared to BD [$F(1,37)=5.49$, p= 0.03, partial $\eta^2= 0.13$]. There were no significant differences in total BIS scores between BD and HC (p>0.05) (Table 2).

CANTAB

MANOVA analyses corrected for age revealed group difference in CGT measures [Pillai's trace F(5,35)=2.8, p=.04, partial η^2=.28]. Quality of decision making [F(1,42)=7.88, p=.008, partial η^2=.17] and risk adjustment [F(1,42)=8.79, p=.005, partial η^2=.18] were significantly reduced in BD compared with HC (p<.01). Further, BD patients displayed increased delay aversion [F(1,42)=5.52, p=.02, partial η^2=.12] (Figure 1).

Performance on the RVP [(Pillai's trace F(3, 30)=1.31, p=.29, partial η^2=.11] and AGN overall mean latencies and accuracy [(Pillai's trace F(2, 38)=.14, p=.87, partial η^2=.007] were comparable across groups. There were also no differences in AGN latencies or accuracy in response to positive and negative stimuli between the two groups (p>0.05; Table 2).

As mentioned in our methods section we covaried all the impulsivity measures found to be statistically significant between BD and HC for potential site and medication effects. Quality of decision making, delay aversion, and risk adjustment were comparable across study sites [F(3,35)=.21, p=.89, η^2=.02], and there was no significant interaction between site and participants' group [F(3,35)=.85, p=.48, η^2=.07]. With regard to medication status CGT scores differed between medicated and unmedicated BD patients [(Pillai's trace F(5, 19)=3.07, p=.03, η^2=.45)]. Specifically, unmedicated BD patients (N=14) displayed better quality of decision-making than medicated BD (N=14) patients [F(1, 23)=5.56, p=.03, η^2=.2)].

Table 2 and Figure 1 about here

Conclusions

To the best of our knowledge this is the first study comparing performance on self-rating and behavioral indicators of impulsivity in older BD patients and a healthy comparison group. The most compelling finding is that older BD patients presented with increased impulsivity as reflected by poor quality of decision making, decreased risk adjustment, and increased delay aversion on the CGT task of the CANTAB battery when compared to a healthy comparison group with no lifetime history of mental illness. Furthermore, medicated BD patients displayed poorer quality of decision making compared to unmedicated individuals. Although promising, these findings are based on a small sample size and should, therefore, be interpreted with caution and be viewed as preliminary.

Our findings are consistent with previous evidence that patients with BD have a high reward-seeking response and are unable to delay gratification (Najt et al., 2007; Swann et al., 2009b). Furthermore, studies using the Cambridge Gambling test of the CANTAB battery (Bauer et al., 2015; Wu et al., 2016) showed that adults with BD display reduced quality of decision making and pronounced risk-taking tendencies. Adult BD patients were also found to discount delayed rewards to a greater extent than healthy controls (Ahn et al., 2011; Mason et al., 2012). Overall, healthy aging has been associated with longer deliberation times and reduced risk taking on a token-based gamble decision

task (Deakin et al., 2004). Similarly, a study showed that, compared to younger adults, older individuals are generally more risk averse and favor future, greater rewards to immediate, smaller rewards (Madden and Bickel, 2010). The greater delay aversion observed in our BD sample may, therefore, indicate that this facet of impulsivity is related to BD rather than just aging.

It is noteworthy mentioning that older adults' ability to discount immediate rewards has been found to apply to monetary rewards but not to liquid rewards (e.g. juice) (Jimura et al., 2011). Along the same line, there is evidence of a strong link between high reactivity to a specific class of rewards and drug-seeking behaviors (Volkow and Wise, 2005) typically comorbid to BD. Examining discounting abilities across reward stimuli (e.g. drugs, food, money) could therefore shed some light into the vulnerability to specific addictive behaviors in older BD patients.

Overall, our older BD patients did not differ from HC in terms of BIS scores, Considering the large number of studies that consistently reported differences in BIS scores in adults with BD (Etain et al., 2013; Strakowski et al., 2010; Swann et al., 2004) and the differences in CGT scores discussed above this finding may be somewhat surprising. To start with, it is important to highlight the fact that impulsivity is a multidimensional concept (Strakowski et al., 2010). Indeed, while BIS is a self-rating measure of motor, attentional, and non-planning impulsivity, the CGT measures the reward-processing component of impulsivity and is based on reaction times and responses to high-reward and low-reward stimuli. A potential reason for the lack of differences on the BIS could, however, be related to insight. Impaired insight into one's abilities (Wood et al., 2012) and health status is a common feature of both mental illness and aging (Cooke et al.,

2005), and is associated with reduced global functioning, medical adherence and worse clinical illness course (van der Werf-Eldering et al., 2011). One could speculate that our sample of older BD patients had reduced insight into their condition and overestimated their ability to inhibit prepotent impulsive behaviors. To check this hypothesis we examined item 11 of the YMRS scale as it assesses insight into the severity of the disease (Young et al., 1978). In our BD sample, raw scores ranged from 0 (excellent insight) to 3 (patient admits change in behavior but denies illness), and the mean value was .19 (S.D=.62). This means that, overall, our BD sample had good insight and admitted to being "possibly" ill. There is therefore no strong evidence supporting the hypothesis that lack of insight explained the greater BIS attentional impulsivity scores reported by HC compared to BD. This remains, however, a surprising result that certainly requires additional exploration.

Alternatively, it could be hypothesized that the BIS is a self-rating measure of "real" daily life impulsivity and that, over time, older BD have "learned" to avoid taking risky decisions with immediate negative impact on their daily life (Carstensen and Hartel, 2006). However, when exposed to an "artificial" measure of impulsivity such as the CGT, older BD patients cannot inhibit their "automatic" impulsive response style, and display risk-seeking behaviors. This hypothesis did not, however, apply to the AGN task as our study did not detect differences in AGN latencies and commission errors in response to affective stimuli between BD and HC. A third explanation for our findings could be based on the concept that aging is associated with reduced attentional bias for negative stimuli, and increased preference for positive information (Mather and Carstensen, 2005; Mroczek and Kolarz, 1998). As a result, in older individuals,

differences in reaction times and accuracy in response to positive and negative stimuli may be reduced. This would explain the current AGN findings and raise the hypothesis that, in elderly BD patients, the reward of “winning a game” triggers a stronger response than the emotional valence of the stimulus *per se*. If this hypothesis were to be confirmed, one could conclude that poor reward-related decision making is intrinsic to BD and persists into late adulthood. Future studies could address this research question by comparing independent (e.g. proxy report) information on the lifetime history and current instances of impulsive behavior to laboratory measures of impulsivity.Whether the reduced response to emotional stimuli observed in our BD sample is a coping strategy or the result of age-related brain and physiological changes (Conwell et al., 1998) remains an unexplored research area.

Notably, in our sample, medicated BD patients displayed poorer quality of decision making on the CGT compared to unmedicated BD individuals. This result is counterintuitive as one would expect that medication would improve mood and potentially mitigate impulsivity. However, our sample took a variety of medications and it is, therefore, difficult to distinguish the impact of each medication on cognition. Lithium has several neuroprotective effects and has been found to have no negative or no effects on cognitive performance in humans. Some animal and human studies have even suggested that lithium may improve learning processes (Adida et al., 2015; Tsaltas et al., 2009). However, anti-convulsants such as carbamazepine and valproate have negative effects on cognition (Gallassi et al., 1990; Hermann et al., 2010). For instance, an animal study showed that carbamazepine impairs processing speed and response accuracy on a decision making task (Tremblay and Winstanley, 2016).

Lamotrigine, a newer generation of anti-convulsants, has less cognitive side effects (Sanches et al., 2014). A confounding factor in the current sample is that with aging, the pharmacokinetics of absorption, metabolism, and excretion of drugs decreases and may lead to increased cognitive side effects (Aziz et al., 2006). Further studies looking at long-term administration of lithium, mood stabilizers and anti-convulsants would be essential to distinguish the effects of different types of medication and BD on reward-related impulsivity measures in older populations.

Equally relevant is the absence of differences in RVP A' (detection scores), RVP B'' (prepotent response tendency), and mean response latency between BD and HC. Although this may seem inconsistent with previous literature (Bora et al., 2007; Malloy-Diniz et al., 2011), it is noteworthy mentioning that previous studies using estimates of signal detection such as A'' and B'', and not only the number of commission errors, found no significant differences between BD and HC (Brooks et al., 2010; Fleck et al., 2005). Further, in this study there was no strong correlation between RVP and BIS scores. This is in line with our previous work that found no significant correlations between the total BIS score and the number of RVP commission errors in a sample of BD with substance use comorbidities (Bauer et al., 2015), and no strong correlations between BIS subscores and RVP A'' and "B'' in young BD patients (Bauer et al., 2017). This evidence provides support for a multidimensional construct of impulsivity and the differential relationship between BIS scores and behavioral measures of impulsivity. For instance, a previous study in adults with BD showed that while high BIS nonplanning and motor impulsivity correlated with poor performance on a gambling task, high BIS

Attentional impulsivity was associated with reduced response inhibition (Christodoulou et al., 2006).

Along with deficits in physical health and poor social functioning, mental health is a significant risk factor for suicide in elderly individuals (Conwell et al., 2002; WHO). Impulsivity is an equally significant predictor of mortality as individuals may make rash, irrational decisions, and put suicidal thoughts and plans into action (Neufeld and O'Rourke, 2009). Evidence shows that inconsistent decision making in situations requiring cognitive complexity and involving long-term, rather than short-term, rewards may contribute to suicidal attempts (Trivedi et al., 2014). Whether impulsivity contributes to suicide to the same extent across the life cycle is, however, still unclear. Some studies suggest that, while in young attempters suicide is an impulsive-aggressive act, suicide in older individuals is a planned and less impulsive act (Conwell et al., 1998; Turecki, 2005). Clark et al. found that older depressed suicide attempters displayed reduced risk-sensitive decision-making and neglected outcome probability when compared non-suicidal depressed patients (Clark et al., 2011). Our sample included 11 BD individuals currently at risk for suicide and 4 individuals who attempted suicide in the past. Given the small size of our BD sample we did not extend our analyses to explore the link between impulsivity and suicidal risk. Future studies should, therefore, focus on whether there are differences in impulsivity, and, based on the current findings, more specifically decision making, between young and older BD patients with and without a history of suicide attempts.

Before drawing final conclusions some limitations need first to be mentioned. The generalizability of the current findings is limited by the small sample size and sample

heterogeneity. Our BD group included participants with BD Type I, II and NOS, half of which were medicated. Previous evidence shows that some aspects of impulsivity differ between BD I and BD II. While BDI may show elevated trait-impulsivity (on the BIS) and lifetime aggression (on the Brown-Goodwin Aggression Scale), BD II are more likely to display increased hostility (measured by the Buss-Durkee Hostility Inventory) (Dervic et al., 2015). As shown in Table 1, our BD sample suffered from a number of comorbidities (e.g. PTSD, eating disorder, generalized anxiety disorder). Given the common comorbidity and some shared symptoms, such as impulsivity, across these psychiatric disorders, it is possible that BD patients with comorbidities display a different impulsivity profile or have greater levels of impulsivity than BD without a history of comorbid disorders. The literature comparing similarities and differences in impulsivity between BD and BD with comorbidities is, however, limited. To address the small sample size limitation we focused our analyses on a number of tasks that were considered to be of relevance for impulsivity. A larger study could, however, include additional measures of both “cold” and “hot” decision making. Furthermore, this study did not measure the levels of anxiety in our sample and these are known to be related to impulsivity in BD (Taylor et al., 2008). The examination of age-related changes in other cognitive domains, such as memory, would have shed light onto additional factors contributing to the decision making process in late adulthood. As mentioned in our methods section, we did not covary our analyses for either chronicity or illness severity. Knowledge of the link between illness severity and impulsivity is limited and somewhat controversial. Two studies found no strong correlation between impulsivity and illness chronicity (Bauer et al., 2015; Swann et al., 2004). By contrast, other findings suggest that an early BD

onset was associated with dysfunctional behaviors (e.g. suicide) often associated with increased impulsivity, and that increased impulsivity was associated with a more severe illness course (Carter et al., 2003; Strakowski et al., 1998; Swann et al., 2009a). The cross-sectional nature of these studies does not, however, enable determining whether there was a causal link between impulsivity and illness course. More research is therefore warranted to clarify how illness severity influences impulsivity. Our sample included both euthymic individuals and individuals meeting DSM-IV criteria for manic, depressive and mixed episodes. Given the relatively small size of each subgroup we could not account for the effects of mood state on impulsivity measures. It is, however, noteworthy to mention that impulsivity has been hypothesized to be a trait rather than a state (Lombardo et al., 2012), and that increased impulsivity has been found to be a risk factor for mania in non-clinical individuals (Johnson et al., 2013). Since the CGT task was the only measure of executive functioning included in this study, future studies should consider including a range of executive measures, including decision-making tasks that do not involve a reward. Furthermore, as previously mentioned, impulsivity is closely related to other cognitive skills such as working memory and attention. Thus, if patients have cognitive impairment, that may affect their ability to make decisions and inhibit responses. The reduced GAF scores observed in our BD samples could also be explored further to determine to what extent impulsivity moderates age-related decline in global functioning (Jiménez et al., 2012).

In summary, our study provided preliminary evidence that elderly BD patients display pronounced risk taking and poor decision making behaviors on a behavioral measure of impulsivity. The lack of differences on a self-rating impulsivity scale between

BD and HC suggests that older BD patients' decisions may be sensitive to context (e.g. self-rated impulsivity in daily life vs laboratory tasks). Additional research in the role of impulsive decision-making in suicide risk and functional outcome in late-life BD may be useful to develop adequate treatment strategies.

Acknowledgements

N/A

References

Adida, M., Jollant, F., Clark, L., Guillaume, S., Goodwin, G.M., Azorin, J.-M., Courtet, P., 2015. Lithium might be associated with better decision-making performance in euthymic bipolar patients. European Neuropsychopharmacology 25, 788-797.
Ahn, W.-Y., Rass, O., Fridberg, D.J., Bishara, A.J., Forsyth, J.K., Breier, A., Busemeyer, J.R., Hetrick, W.P., Bolbecker, A.R., O'donnell, B.F., 2011. Temporal discounting of rewards in patients with bipolar disorder and schizophrenia. Journal of abnormal psychology 120, 911.
Almeida, O.P., Hankey, G.J., Yeap, B.B., Golledge, J., Hill, K.D., Flicker, L., 2016. Depression Among Nonfrail Old Men Is Associated With Reduced Physical Function and Functional Capacity After 9 Years Follow-up: The Health in Men Cohort Study. Journal of the American Medical Directors Association.
Aziz, R., Lorberg, B., Tampi, R.R., 2006. Treatments for late-life bipolar disorder. The American journal of geriatric pharmacotherapy 4, 347-364.
Bauer, I.E., Meyer, T.D., Sanches, M., Spiker, D., Zunta-Soares, G., Soares, J.C., 2017. Are self-rated and behavioural measures of impulsivity in bipolar disorder mainly related to comorbid substance use problems? Cognitive neuropsychiatry, 1-17.
Bauer, I.E., Meyer, T.D., Sanches, M., Zunta-Soares, G., Soares, J.C., 2015. Does a history of substance abuse and illness chronicity predict increased impulsivity in bipolar disorder? Journal of affective disorders 179, 142-147.
Bechara, A., 2005. Decision making, impulse control and loss of willpower to resist drugs: a neurocognitive perspective. Nature neuroscience 8, 1458-1463.
Bland, J.M., Altman, D.G., 1995. Multiple significance tests: the Bonferroni method. Bmj 310, 170.
Bora, E., Vahip, S., Akdeniz, F., Gonul, A.S., Eryavuz, A., Ogut, M., Alkan, M., 2007. The effect of previous psychotic mood episodes on cognitive impairment in euthymic bipolar patients. Bipolar disorders 9, 468-477.
Brooks, J.O., Bearden, C.E., Hoblyn, J.C., Woodard, S.A., Ketter, T.A., 2010. Prefrontal and paralimbic metabolic dysregulation related to sustained attention in euthymic older adults with bipolar disorder. Bipolar disorders 12, 866-874.
Brown, L.A., Brockmole, J.R., Gow, A.J., Deary, I.J., 2012. Processing speed and visuospatial executive function predict visual working memory ability in older adults. Experimental aging research 38, 1-19.
Carstensen, L.L., Hartel, C.R., 2006. When I'm 64. National Academies Press.
Carter, T.D.C., Mundo, E., Parikh, S.V., Kennedy, J.L., 2003. Early age at onset as a risk factor for poor outcome of bipolar disorder. Journal of psychiatric research 37, 297-303.
Carver, C.S., White, T.L., 1994. Behavioral inhibition, behavioral activation, and affective responses to impending reward and punishment: the BIS/BAS scales. Journal of personality and social psychology 67, 319.
CDC., 2008. The State of Mental Health and Aging in America. Issue Brief 1: What Do the Data Tell Us? . National Association of Chronic Disease Directors, Atlanta, GA.
Chamberlain, S.R., Sahakian, B.J., 2007. The neuropsychiatry of impulsivity. Current Opinion in Psychiatry 20, 255-261.

Chamorro, J., Bernardi, S., Potenza, M.N., Grant, J.E., Marsh, R., Wang, S., Blanco, C., 2012. Impulsivity in the general population: a national study. Journal of psychiatric research 46, 994-1001.
Chapman, D.P., Perry, G.S., Strine, T.W., 2005. The vital link between chronic disease and depressive disorders. Prev Chronic Dis 2, A14.
Cheema, M.K., MacQueen, G.M., Hassel, S., 2015. Assessing personal financial management in patients with bipolar disorder and its relation to impulsivity and response inhibition. Cognitive neuropsychiatry 20, 424-437.
Christodoulou, T., Lewis, M., Ploubidis, G., Frangou, S., 2006. The relationship of impulsivity to response inhibition and decision-making in remitted patients with bipolar disorder. European Psychiatry 21, 270-273.
Clark, L., Dombrovski, A.Y., Siegle, G.J., Butters, M.A., Shollenberger, C.L., Sahakian, B.J., Szanto, K., 2011. Impairment in risk-sensitive decision-making in older suicide attempters with depression. Psychology and aging 26, 321.
Conwell, Y., Duberstein, P.R., Caine, E.D., 2002. Risk factors for suicide in later life. Biological psychiatry 52, 193-204.
Conwell, Y., Duberstein, P.R., Cox, C., Herrmann, J., Forbes, N., Caine, E.D., 1998. Age differences in behaviors leading to completed suicide. The American Journal of Geriatric Psychiatry 6, 122-126.
Cooke, M., Peters, E., Kuipers, E., Kumari, V., 2005. Disease, deficit or denial? Models of poor insight in psychosis. Acta Psychiatrica Scandinavica 112, 4-17.
Coyne, A.C., Whitbourne, S.K., Glenwick, D.S., 1978. Adult age differences in reflection-impulsivity. Journal of gerontology 33, 402-407.
Daglas, R., Cotton, S., Allott, K., Yücel, M., Macneil, C., Hasty, M., Murphy, B., Pantelis, C., Hallam, K., Henry, L., 2016. A single-blind, randomised controlled trial on the effects of lithium and quetiapine monotherapy on the trajectory of cognitive functioning in first episode mania: A 12-month follow-up study. European Psychiatry 31, 20-28.
Deakin, J., Aitken, M., Robbins, T., Sahakian, B.J., 2004. Risk taking during decision-making in normal volunteers changes with age. Journal of the International Neuropsychological Society 10, 590-598.
Depp, C.A., Savla, G.N., Moore, D.J., Palmer, B.W., Stricker, J.L., Lebowitz, B.D., Jeste, D.V., 2008. Short-term course of neuropsychological abilities in middle-aged and older adults with bipolar disorder. Bipolar disorders 10, 684-690.
Dervic, K., Garcia-Amador, M., Sudol, K., Freed, P., Brent, D., Mann, J., Harkavy-Friedman, J., Oquendo, M., 2015. Bipolar I and II versus unipolar depression: clinical differences and impulsivity/aggression traits. European Psychiatry 30, 106-113.
Dhingra, U., Rabins, P.V., 1991. Mania in the Elderly: A 5–7 Year Follow-Up. Journal of the American Geriatrics Society 39, 581-583.
Drobetz, R., Maercker, A., Forstmeier, S., 2012. Delay of gratification in old age: assessment, age-related effects, and clinical implications. Aging clinical and experimental research 24, 6-14.
Ernst, M., Dickstein, D.P., Munson, S., Eshel, N., Pradella, A., Jazbec, S., Pine, D.S., Leibenluft, E., 2004. Reward-related processes in pediatric bipolar disorder: a pilot study. Journal of Affective Disorders 82, S89-S101.
Etain, B., Mathieu, F., Liquet, S., Raust, A., Cochet, B., Richard, J.R., Gard, S., Zanouy, L., Kahn, J.P., Cohen, R.F., Bougerol, T., Henry, C., Leboyer, M., Bellivier, F., 2013. Clinical features associated with trait-impulsiveness in euthymic bipolar disorder patients. J Affect Disord 144, 240-247.
Ethridge, L.E., Soilleux, M., Nakonezny, P.A., Reilly, J.L., Hill, S.K., Keefe, R.S., Gershon, E.S., Pearlson, G.D., Tamminga, C.A., Keshavan, M.S., 2014. Behavioral response inhibition in psychotic disorders: diagnostic specificity, familiality and relation to generalized cognitive deficit. Schizophrenia research 159, 491-498.

Fleck, D.E., Shear, P.K., Strakowski, S.M., 2005. Processing efficiency and sustained attention in bipolar disorder. Journal of the International Neuropsychological Society 11, 49-57.
Forstmeier, S., Drobetz, R., Maercker, A., 2011. The delay of gratification test for adults: Validating a behavioral measure of self-motivation in a sample of older people. Motivation and Emotion 35, 118-134.
Fung, C.H., Vitiello, M.V., Alessi, C.A., Kuchel, G.A., 2016. Report and Research Agenda of the American Geriatrics Society and National Institute on Aging Bedside-to-Bench Conference on Sleep, Circadian Rhythms, and Aging: New Avenues for Improving Brain Health, Physical Health, and Functioning. Journal of the American Geriatrics Society 64.
Gallassi, R., Morreale, A., Lorusso, S., Procaccianti, G., Lugaresi, E., Baruzzi, A., 1990. Cognitive effects of valproate. Epilepsy research 5, 160-164.
Gildengers, A.G., Mulsant, B.H., Begley, A., Mazumdar, S., Hyams, A.V., Reynolds III, C.F., Kupfer, D.J., Butters, M.A., 2009. The longitudinal course of cognition in older adults with bipolar disorder. Bipolar disorders 11, 744-752.
Gruber, S., Rathgeber, K., Bräunig, P., Gauggel, S., 2007. Stability and course of neuropsychological deficits in manic and depressed bipolar patients compared to patients with major depression. Journal of Affective Disorders 104, 61-71.
Hermann, B., Meador, K.J., Gaillard, W.D., Cramer, J.A., 2010. Cognition across the lifespan: antiepileptic drugs, epilepsy, or both? Epilepsy & Behavior 17, 1-5.
Jiménez, E., Arias, B., Castellví, P., Goikolea, J., Rosa, A., Fananas, L., Vieta, E., Benabarre, A., 2012. Impulsivity and functional impairment in bipolar disorder. Journal of affective disorders 136, 491-497.
Jimura, K., Myerson, J., Hilgard, J., Keighley, J., Braver, T.S., Green, L., 2011. Domain independence and stability in young and older adults' discounting of delayed rewards. Behavioural processes 87, 253-259.
Johnson, S.L., 2005. Mania and dysregulation in goal pursuit: A review. Clinical psychology review 25, 241-262.
Johnson, S.L., Carver, C.S., Mulé, S., Joormann, J., 2013. Impulsivity and risk for mania: Towards greater specificity. Psychology and Psychotherapy: Theory, Research and Practice 86, 401-412.
Jorm, A.F., Christensen, H., Henderson, A.S., Jacomb, P.A., Korten, A.E., Rodgers, B., 1998. Using the BIS/BAS scales to measure behavioural inhibition and behavioural activation: Factor structure, validity and norms in a large community sample. Personality and Individual Differences 26, 49-58.
Lai, F.D., Ip, A.K., Lee, T.M., 2011. Impulsivity and pathological gambling: Is it a state or a trait problem? BMC research notes 4, 492.
Leibenluft, E., Rich, B.A., Vinton, D.T., Nelson, E.E., Fromm, S.J., Berghorst, L.H., Joshi, P., Robb, A., Schachar, R.J., Dickstein, D.P., 2007. Neural circuitry engaged during unsuccessful motor inhibition in pediatric bipolar disorder. American Journal of Psychiatry 164, 52-60.
Lewandowski, K.E., Sperry, S.H., Malloy, M.C., Forester, B.P., 2014. Age as a predictor of cognitive decline in bipolar disorder. The American Journal of Geriatric Psychiatry 22, 1462-1468.
Linke, J., King, A.V., Rietschel, M., Strohmaier, J., Hennerici, M., Gass, A., Meyer-Lindenberg, A., Wessa, M., 2012. Increased medial orbitofrontal and amygdala activation: evidence for a systems-level endophenotype of bipolar I disorder. American Journal of Psychiatry 169, 316-325.
Linke, J., Sönnekes, C., Wessa, M., 2011. Sensitivity to positive and negative feedback in euthymic patients with bipolar I disorder: the last episode makes the difference. Bipolar disorders 13, 638-650.
Lombardo, L.E., Bearden, C.E., Barrett, J., Brumbaugh, M.S., Pittman, B., Frangou, S., Glahn, D.C., 2012. Trait impulsivity as an endophenotype for bipolar I disorder. Bipolar disorders 14, 565-570.
Madden, G.J., Bickel, W.K., 2010. Impulsivity: The behavioral and neurological science of discounting. American Psychological Association.
Malloy-Diniz, L.F., Neves, F.S., de Moraes, P.H.P., De Marco, L.A., Romano-Silva, M.A., Krebs, M.-O., Corrêa, H., 2011. The 5-HTTLPR polymorphism, impulsivity and suicide behavior in euthymic bipolar patients. Journal of affective disorders 133, 221-226.

Mason, L., O'Sullivan, N., Blackburn, M., Bentall, R., El-Deredy, W., 2012. I want it now! Neural correlates of hypersensitivity to immediate reward in hypomania. Biological psychiatry 71, 530-537.
Mason, L., O'Sullivan, N., Montaldi, D., Bentall, R.P., El-Deredy, W., 2014. Decision-making and trait impulsivity in bipolar disorder are associated with reduced prefrontal regulation of striatal reward valuation. Brain, awu152.
Mather, M., Carstensen, L.L., 2005. Aging and motivated cognition: The positivity effect in attention and memory. Trends in cognitive sciences 9, 496-502.
Meda, S.A., Stevens, M.C., Potenza, M.N., Pittman, B., Gueorguieva, R., Andrews, M.M., Thomas, A.D., Muska, C., Hylton, J.L., Pearlson, G.D., 2009. Investigating the behavioral and self-report constructs of impulsivity domains using principal component analysis. Behavioural pharmacology 20, 390.
Meyer, T.D., Hautzinger, M., 2001. Hypomanic personality, social anhedonia and impulsive nonconformity: evidence for familial aggregation? Journal of personality disorders 15, 281-299.
Mezuk, B., Gallo, J., 2013. Depression and medical illness in late life: race, resources, and stress. Late-life mood disorders. Oxford: Oxford University Press.
Montgomery, S.A., Asberg, M., 1979. A new depression scale designed to be sensitive to change. The British journal of psychiatry 134, 382-389.
Morales-Vives, F., Vigil-Colet, A., 2012. Are old people so gentle? Functional and dysfunctional impulsivity in the elderly. International Psychogeriatrics 24, 465-471.
Mroczek, D.K., Kolarz, C.M., 1998. The effect of age on positive and negative affect: a developmental perspective on happiness. Journal of personality and social psychology 75, 1333.
Murphy, F., Sahakian, B., Rubinsztein, J., Michael, A., Rogers, R., Robbins, T., Paykel, E., 1999. Emotional bias and inhibitory control processes in mania and depression. Psychological medicine 29, 1307-1321.
Najt, P., Perez, J., Sanches, M., Peluso, M., Glahn, D., Soares, J.C., 2007. Impulsivity and bipolar disorder. European Neuropsychopharmacology 17, 313-320.
Neufeld, E., O'Rourke, N., 2009. Impulsivity and hopelessness as predictors of suicide-related ideation among older adults. The Canadian Journal of Psychiatry 54, 684-692.
Nusslock, R., Almeida, J.R., Forbes, E.E., Versace, A., Frank, E., LaBarbara, E.J., Klein, C.R., Phillips, M.L., 2012. Waiting to win: elevated striatal and orbitofrontal cortical activity during reward anticipation in euthymic bipolar disorder adults. Bipolar disorders 14, 249-260.
Patton, J.H., Stanford, M.S., 1995. Factor structure of the Barratt impulsiveness scale. Journal of clinical psychology 51, 768-774.
Powers, R.L., Russo, M., Mahon, K., Brand, J., Braga, R.J., Malhotra, A.K., Burdick, K.E., 2013. Impulsivity in bipolar disorder: relationships with neurocognitive dysfunction and substance use history. Bipolar disorders 15, 876-884.
Robbins, T.W., James, M., Owen, A.M., Sahakian, B.J., Lawrence, A.D., McInnes, L., RABBITT, P.M., 1998. A study of performance on tests from the CANTAB battery sensitive to frontal lobe dysfunction in a large sample of normal volunteers: Implications for theories of executive functioning and cognitive aging. Journal of the International Neuropsychological Society 4, 474-490.
Roiser, J.P., Cannon, D.M., Gandhi, S.K., Tavares, J.T., Erickson, K., Wood, S., Klaver, J.M., Clark, L., Zarate Jr, C.A., Sahakian, B.J., 2009. Hot and cold cognition in unmedicated depressed subjects with bipolar disorder. Bipolar disorders 11, 178-189.
Sabater, A., García-Blanco, A.C., Verdet, H.M., Sierra, P., Ribes, J., Villar, I., Lara, M.J., Arnal, P., Rojo, L., Livianos, L., 2016. Comparative neurocognitive effects of lithium and anticonvulsants in long-term stable bipolar patients. Journal of affective disorders 190, 34-40.
Salgado, J.V., Malloy-Diniz, L.F., Campos, V.R., Abrantes, S.S.C., Fuentes, D., Bechara, A., Correa, H., 2009. Neuropsychological assessment of impulsive behavior in abstinent alcohol-dependent subjects. Revista Brasileira de Psiquiatria 31, 4-9.

Sanches, M., Bauer, I.E., Galvez, J.F., Zunta-Soares, G.B., Soares, J.C., 2014. The management of cognitive impairment in bipolar disorder: current status and perspectives. American journal of therapeutics 22, 477-486.
Sarapas, C., Shankman, S.A., Harrow, M., Goldberg, J.F., 2012. Parsing trait and state effects of depression severity on neurocognition: Evidence from a 26-year longitudinal study. Journal of abnormal psychology 121, 830.
Schouws, S.N., Comijs, H.C., Dols, A., Beekman, A.T., Stek, M.L., 2016. Five-year follow-up of cognitive impairment in older adults with bipolar disorder. Bipolar disorders.
Schouws, S.N., Stek, M.L., Comijs, H.C., Dols, A., Beekman, A.T., 2012. Cognitive decline in elderly bipolar disorder patients: a follow-up study. Bipolar disorders 14, 749-755.
Simon, G.E., Hunkeler, E., Fireman, B., Lee, J.Y., Savarino, J., 2007. Risk of suicide attempt and suicide death in patients treated for bipolar disorder1. Bipolar disorders 9, 526-530.
Strakowski, S.M., Fleck, D.E., DelBello, M.P., Adler, C.M., Shear, P.K., Kotwal, R., Arndt, S., 2010. Impulsivity across the course of bipolar disorder. Bipolar disorders 12, 285-297.
Strakowski, S.M., Sax, K.W., McElroy, S.L., Keck Jr, P.E., Hawkins, J.M., West, S.A., 1998. Course of psychiatric and substance abuse syndromes co-occurring with bipolar disorder after a first psychiatric hospitalization. The Journal of clinical psychiatry 59, 465-471.
Swann, A.C., Dougherty, D.M., Pazzaglia, P.J., Pham, M., Moeller, F.G., 2004. Impulsivity: a link between bipolar disorder and substance abuse. Bipolar disorders 6, 204-212.
Swann, A.C., Lijffijt, M., Lane, S.D., Steinberg, J.L., Moeller, F.G., 2009a. Increased trait-like impulsivity and course of illness in bipolar disorder. Bipolar disorders 11, 280-288.
Swann, A.C., Lijffijt, M., Lane, S.D., Steinberg, J.L., Moeller, F.G., 2009b. Severity of bipolar disorder is associated with impairment of response inhibition. Journal of Affective Disorders 116, 30-36.
Sweeney, J.A., Kmiec, J.A., Kupfer, D.J., 2000. Neuropsychologic impairments in bipolar and unipolar mood disorders on the CANTAB neurocognitive battery. Biological psychiatry 48, 674-684.
Taylor, C.T., Hirshfeld-Becker, D.R., Ostacher, M.J., Chow, C.W., LeBeau, R.T., Pollack, M.H., Nierenberg, A.A., Simon, N.M., 2008. Anxiety is associated with impulsivity in bipolar disorder. Journal of Anxiety Disorders 22, 868-876.
Tremblay, M., Winstanley, C.A., 2016. Anticonvulsant medications attenuate amphetamine-induced deficits in behavioral inhibition but not decision making under risk on a rat gambling task. Behavioural brain research 314, 143-151.
Trivedi, S.C., Shetty, N.K., Raut, N.B., Subramanyam, A.A., Shah, H.R., Pinto, C., 2014. Study of suicidal ideations, hopelessness and impulsivity in elderly. Journal of Geriatric Mental Health 1, 38.
Tsaltas, E., Kontis, D., Boulougouris, V., Papadimitriou, G.N., 2009. Lithium and cognitive enhancement: leave it or take it? Psychopharmacology 202, 457-476.
Turecki, G., 2005. Dissecting the suicide phenotype: the role of impulsive-aggressive behaviours. Journal of psychiatry & neuroscience: JPN 30, 398.
van der Werf-Eldering, M.J., van der Meer, L., Burger, H., Holthausen, E.A., Nolen, W.A., Aleman, A., 2011. Insight in bipolar disorder: associations with cognitive and emotional processing and illness characteristics. Bipolar disorders 13, 343-354.
Volkow, N.D., Wise, R.A., 2005. How can drug addiction help us understand obesity? Nature neuroscience 8, 555-560.
Walshaw, P.D., Alloy, L.B., Sabb, F.W., 2010. Executive function in pediatric bipolar disorder and attention-deficit hyperactivity disorder: in search of distinct phenotypic profiles. Neuropsychology review 20, 103-120.
Wechsler, D., 1999. WASI (Wechsler Adult Scale–reduced). New York: The Psychological Corporation.

WHO,
http://www.who.int/gho/publications/world_health_statistics/2016/whs2016_AnnexA_Suicide.pdf?ua=1&ua=1 [Last accessed on 2016 Oct 10].
Wood, J.M., Lacherez, P.F., Anstey, K.J., 2012. Not all older adults have insight into their driving abilities: evidence from an on-road assessment and implications for policy. Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences 68, 559-566.
Wu, M.-J., Passos, I.C., Bauer, I.E., Lavagnino, L., Cao, B., Zunta-Soares, G.B., Kapczinski, F., Mwangi, B., Soares, J.C., 2016. Individualized identification of euthymic bipolar disorder using the Cambridge Neuropsychological Test Automated Battery (CANTAB) and machine learning. Journal of affective disorders 192, 219-225.
Young, R., Biggs, J., Ziegler, V., Meyer, D., 1978. A rating scale for mania: reliability, validity and sensitivity. The British Journal of Psychiatry 133, 429-435.

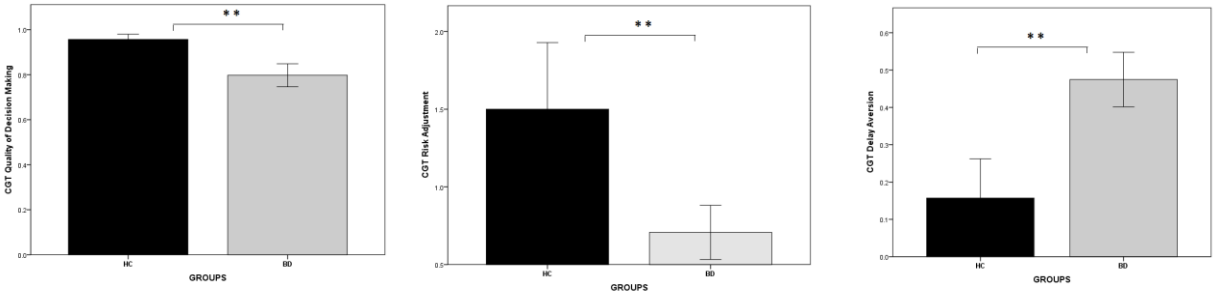

Figure 1. Mean Risk Adjustment, Quality Decision Making, and Delay Aversion scores of the Cambridge Gambling task (CGT) in BD and HC. BD displayed decreased quality of decision making and risk adjustment, and increased delay aversion. **:p<.01

Table 1: Demographic and clinical characteristic of healthy controls (HC) and individuals with bipolar disorder (BD)

Group	HC Mean±S.D.	BD Mean±S.D.	F/chi square	p-value
N	15	28		
Age (years)	55.1±3.95	56.07±4.08	.56	.46
Sex (N women)	6	16	.35	.23
BD subtype		19 BDI, 6BDII, 3 BDNOS		
Education (years)	17.07±3.37	14.36±.1.87	11.6	**<.01**
Medication status (N medicated individuals)	0	14		
Type of medication		11 polymedication (5 of which took lithium), 1 anticonvulsant,1 antipsychotic, 1 benzodiazepine		
Current mood state		9 euthymic 10 depressed 2 manic 1 hypomanic 1 mixed		
Age BD diagnosis (years)		41.43±11.45		
Current suicide risk (N)		4		
Past suicidal risk (N)		11		
Number of hospitalizations *Median* *Range of values*		1.6±1.8 1 0-5		
Number of mood episodes *Median* *Range of values*		26.67±31.3 9 0-70		
MADRS *Median* *Range of values*	.33±.62 0 0-2	16.96±12.04 18 0-35	28.09	**<.001**
YMRS *Median* *Range of values*	.33±.62 0 0-2	5.68±5.84 4 0-20	10.19	**<.01**
Comorbidities		11 had multi comorbidities (e.g. PTSD,ED, SUD), 1 suffered from PTSD, 2 from GAD NOS, and 2		

Table 2: Self-rating and behavioral measures of impulsivity for healthy controls (HC) and individuals with bipolar disorder (BD).

Group	HC Mean±S.D.	BD Mean±S.D.	F	p-value	Partial η^2
N	15	28			
BIS#					
BIS Attentional	23.31±1.55	21.52±2.47	5.49	**.03**	.13
BIS Motor	24.92±2.5	26±3.13	.85	.36	.02
BIS Non-planning	24.31±3.28	26.41±4.41	1.86	.18	.05
Total BIS	72.54±3.73	73.93±4.48	.53	.47	.01
AGN					
Latency Correct trials (ms)	557.55±74.74	572.58±60.44	.25	.62	.01
Total commission errors	20.07±10.25	19.36±15.37	.06	.81	.001
Latency Correct trials–positive (ms)	540.76±69.95	553.91±54.65	.26	.61	.01
Total commission errors-positive	3.57±1.64	3.48±3.09	.03	.86	.001
Latency Correct trials–negative (ms)	541.17±81.39	561.47±65.69	.49	.49	.012
Total commission errors-negative	2.28±2.29	2.77±2.66	.49	.49	.012
CGT					
Delay aversion	.23±.17	.43±.28	5.516	**.02**	.12
Deliberation Time (ms)	2480.44±791.68	2839.01±1242.36	.9	.35	.02
Quality of Decision Making	.96±.06	.84±.20	7.88	**.01**	.17
Risk Adjustment	1.49±.96	.74±.68	8.79	**.01**	.18
Risk Taking	.56±.14	.54±.17	.15	.7	.004
RVP##					
RVP A’	.93±.03	.9±.05	4.03	**.05**	.11
RVP B’’	.98±.03	.91±.22	.87	.36	.03
Latency (ms)	427.58±87.75	469.83±99.49	1.46	.24	.04

Abbreviations: AGN: Affective Go/No-Go; BIS: Barratt Impulsivity Scale; CGT: Cambridge Gambling Task; RVP: Rapid Visual Processing

-Cross-sectional study comparing impulsive behavior in older BD and HC

-BD displayed poor decision making, risk taking, and increased delay aversion compared to HC

-Self-rating measures of impulsivity were comparable between BD and HC

-In BD impulsive reward-based decision making persist into late adulthood