Psychological Medicine

cambridge.org/psm

Impulsivity, decision-making and risk-taking behaviour in bipolar disorder: a systematic review and meta-analysis

Almudena Ramírez-Martín[1], Javier Ramos-Martín[1], Fermin Mayoral-Cleries[2], Berta Moreno-Küstner[1] and Jose Guzman-Parra[2]

[1]Departamento de Personalidad, Evaluación y Tratamiento Psicológico, Grupo GAP, Facultad de Psicología, Universidad de Málaga, Malaga, Spain and [2]Department of Mental Health, University General Hospital of Malaga. Biomedical Research Institute of Malaga (IBIMA), Malaga, Spain

Review Article

Cite this article: Ramírez-Martín A, Ramos-Martín J, Mayoral-Cleries F, Moreno-Küstner B, Guzman-Parra J (2020). Impulsivity, decision-making and risk-taking behaviour in bipolar disorder: a systematic review and meta-analysis. *Psychological Medicine* **50**, 2141–2153. https://doi.org/10.1017/S0033291720003086

Received: 30 September 2019
Revised: 6 May 2020
Accepted: 11 August 2020
First published online: 3 September 2020

Key words:
Bipolar disorder; decision-making; impulsivity; meta-analysis; risk-taking behaviour; systematic review

Author for correspondence:
Jose Guzman-Parra,
E-mail: joseguzman@uma.es

Abstract

Despite the robust body of work on cognitive aspects of bipolar disorder (BD), a clear profile of associated impairments in impulsivity, decision-making and risk-taking from studies that use behavioural measures has yet to be established. A systematic review, across four electronic databases (PsycINFO, MEDLINE/PubMed, ScienceDirect and Scopus), of literature published between January 1999 and December 2018 was carried out in accordance with the PRISMA statement. The protocol was registered on PROSPERO (CRD42018114684). A fixed-effect and random-effects meta-analysis using the Hedges' g (ES) estimate was performed. The analysis revealed significant impairment in BD individuals with medium effect sizes in various aspects of impulsivity – response inhibition (ES = 0.49; $p < 0.0001$), delay of gratification (ES = 0.54; $p < 0.0001$) and inattention (ES = 0.49; $p < 0.0001$) – and in decision-making (ES = 0.61, $p = 0.0002$), but no significant impairment in risk-taking behaviour (ES = 0.41; $p = 0.0598$). Furthermore, we found significant heterogeneity between studies for decision-making and risk-taking behaviour but not for impulsivity. Impaired risk-taking behaviour was significant in a subgroup of BD-I and euthymic individuals (ES = 0.92; $p < 0.0001$) with no significant heterogeneity. A stratification analysis revealed comparable results in euthymic and non-euthymic individuals for impulsivity. Our findings suggest that behaviour impulsivity is elevated in all phases of BD, representing a core and clinically relevant feature that persists beyond mood symptoms. More studies about decision-making and risk-taking are necessary to establish if they are impaired in BD and to analyze the role of mood state.

Introduction

Bipolar disorder (BD) is a complex mental disorder with multidimensional psychopathology and lifetime prevalence rates estimated at approximately 2–4% (Ketter, 2010; Merikangas et al., 2011). Growing evidence has revealed that patients with BD exhibit prominent cognitive impairment, especially in the domains of executive function (Grande, Berk, Birmaher, & Vieta, 2016; Miskowiak et al., 2017). This executive dysfunction includes abnormalities in impulsivity, decision-making and risk-taking behaviours among others. Thus, high levels of impulsivity, sub-optimal decision-making and potentially dangerous risky behaviours appear to be frequent components in the course of BD in its various phases and have been proposed as promising endophenotypes (core features) of the disease (Chamorro et al., 2012; Christodoulou, Lewis, Ploubidis, & Frangou, 2006; Najt et al., 2007).

Impulsivity is a multidimensional construct that can be defined as a predisposition to rapid, unplanned reactions to internal or external stimuli that fail to take into account the negative consequences of those reactions to the individual him-/herself or to others (Moeller, Barratt, Dougherty, Schmitz, & Swann, 2001). Some authors have suggested that behavioural manifestations of this domain include three different components: (a) response inhibition: involving the ability to withhold a speeded motor response prior to its initiation or the ability to cancel a response after it has been initiated (Wright, Lipszyc, Dupuis, Thayapararajah, & Schachar, 2014); (b) delay of gratification: preference for immediately-available small rewards *v.* large but delayed rewards; and (c) inattention: the inability to maintain one's attention in order to complete a task without being distracted (Strakowski et al., 2009, 2010). An extensive body of research has studied the multiple dimensions of this domain using self-report measures (e.g. the Barratt Impulsivity Scale); conversely, studies that have explored impulsivity using laboratory-based behavioural measures are limited and their results somewhat are contradictory (Christodoulou et al., 2006; Powers et al., 2013). To our knowledge, no meta-analysis has specifically investigated behavioural impulsivity in BD, and only two previous reviews have included studies that used both self-report and cognitive tasks measures. For

© The Author(s), 2020. Published by Cambridge University Press

CAMBRIDGE UNIVERSITY PRESS

example, Najt et al. (2007) found self-reported impulsivity to be higher among BD patients compared with healthy controls, regardless of the phase of the illness. A second review explored impulsivity in the euthymic stage of BD, analysing both self-reported impulsivity and two commonly identified behavioural manifestations of impulsivity: response inhibition and the ability to delay gratification (Newman & Meyer, 2014). It is found that most studies using self-report measures reported significant differences between euthymic BD patients and healthy controls, whereas there was little evidence of higher impulsivity when measured by behavioural paradigms. Therefore, although there is consistent evidence that patients with BD report higher impulsivity when self-ratings are used (Najt et al., 2007; Saddichha & Schuetz, 2014), the evidence when behavioural paradigms are applied is contradictory.

Decision-making impairment has also been a persistent finding in BD. This construct is defined as a complex set of cognitive processes which allow individuals to select the most optimal course of action following consideration of existing alternatives (Bechara, 2005). Recent studies have identified at least two distinct forms of reward-based decision making: (a) decision-making under risk, measured by performance in tasks with explicit outcome probabilities; and (b) decision-making under ambiguity, measured by performance in tasks with implicit outcome probabilities (Wilson & Vassileva, 2018). Overall, studies tended to report poorer outcomes on decision-making in BD patients compared with healthy controls (Powers et al., 2013; Roiser et al., 2009), but contrary results have also been found. A meta-analysis by Samamé, Martino, and Strejilevich (2012) found decision-making abilities to be preserved in patients with euthymic BD. In the same vein, the findings of a later meta-analysis (Edge, Johnson, Ng, & Carver, 2013) indicated that bipolar and control groups do not differ on the total number of risky choices they make. It is important to point out that both studies only investigated the euthymic phase and did not investigate either mania or depression states. A third meta-analysis, however, suggested the existence of various cognitive profiles of decision-making in patients diagnosed with BD (Jiménez et al., 2018). Hence, decision-making ability in BD patients remains unclear, and to date, no meta-analytic studies have reviewed the findings of empirical studies of the three phases of the disorder.

Finally, although risk-taking behaviour is often part of the clinical presentation of BD, very few studies have formally assessed risk-taking propensity in these patients. A popular laboratory procedure used for studying risk-taking involves gambling tasks, where subjects are asked to choose between safe and risky alternatives. Participants can usually choose among several options that differ in the chance for a reward or penalty. The exact probability distribution of the outcome can be evident for the participant (explicit) or not (implicit). Among the few studies that use these gambling tasks, the findings are inconsistent (Chamorro et al., 2012; Holmes et al., 2009). Likewise, no meta-analysis or review has tried to integrate the various findings. Consequently, our knowledge of risk-taking behaviour in BD patients understood as situationally determined behaviours with a high potential for harm or loss and simultaneous opportunity to obtain some form of reward (Leigh, 1999), is still scant.

Despite the robust body of work on cognitive aspects of BD, a clear profile of deficits in associated impulsivity, decision-making and risk-taking behaviour in BD patients has yet to be established. The aim of this study was to conduct a systematic review and meta-analysis of the degree of impairment of these domains in individuals with BD during symptomatic and remitted states, focusing on studies that used a behavioural paradigm. By considering behavioural measures only, our study provides objective results – thereby avoiding the possible biases related to the subjectivity that self-report measures entail – as well as information on certain facets that questionnaires do not detect. Understanding the extent to which impulsivity, decision-making and risk-taking behaviour are affected in individuals with BD will help us to better define the cognitive profile and core features of this disorder.

Methodology

Identification of the studies

We performed a systematic review and a meta-analysis in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) statement (Moher, Liberati, Tetzlaff, & Altman, 2009). The protocol was registered in the PROSPERO database (CRD42018114684). Two investigators (AR and JR) independently conducted literature searches on the PsycINFO, PubMed, ScienceDirect and Scopus databases during the period October–December 2018. Three independent searches were performed on each database, according to the following title/abstract sections: '*impulsivity* OR *impulsive behaviour* OR *impulsiveness* AND *bipolar disorder*'; '*decision-making* AND *bipolar disorder*'; '*risk behaviour* OR *risk-taking* AND *bipolar disorder*'. All papers published in either English or Spanish between January 1999 and December 2018 were considered.

The following inclusion criteria were applied: (a) type of study: cohort or case-control studies; (b) age range: adult subjects (aged 18–70 years); (c) diagnosis: any bipolar disorder (BD-I, BD-II, BD-NOS) in any of its phases (mania, depression or euthymia) diagnosed using internationally accepted assessment instruments, including clinical interviews that applied the criteria of the Diagnostic and Statistical Manual of Mental Disorders (DSM) or the International Statistical Classification of Diseases and Related Health Problems (ICD); (d) evaluation of cognitive domains performed using behavioural measures; (e) published during the period 1999–2018; (f) language: English or Spanish only. The following exclusion criteria were applied: (a) narrative or systematic reviews, qualitative or case studies; (b) children, the young and the elderly (i.e. <18 years and >70 years); (c) adult subjects with any other psychiatric disorder; (d) studies assessing impulsivity as a personality trait; (e) studies evaluating the cognitive domain using questionnaires or self-reports; (f) studies using non-standardised tests; (g) studies whose data were duplicated or not original; (h) studies offering no data for meta-analysis.

The search of the databases generated 2206 results. A further two studies were identified after searching the references of the selected articles. We excluded 1152 duplicate articles, leaving 1056 to be reviewed by title and abstract. Of these, 996 were excluded because they did not meet the inclusion criteria. Of the remaining 60 full-text articles, 30 were excluded for the following reasons: (a) no original data ($n = 5$); (b) no behavioural measures ($n = 3$); (c) use of non-standardised tests ($n = 4$); (d) no BD diagnosis ($n = 1$); (e) use of a duplicate sample ($n = 8$); (f) no data for meta-analysis ($n = 8$); and (g) outcome measure not valid ($n = 1$). More detailed information about the excluded studies is shown in the online Supplementary Table S1. Any differences of opinion as to which studies were to be included or

https://doi.org/10.1017/S0033291720003086 Published online by Cambridge University Press

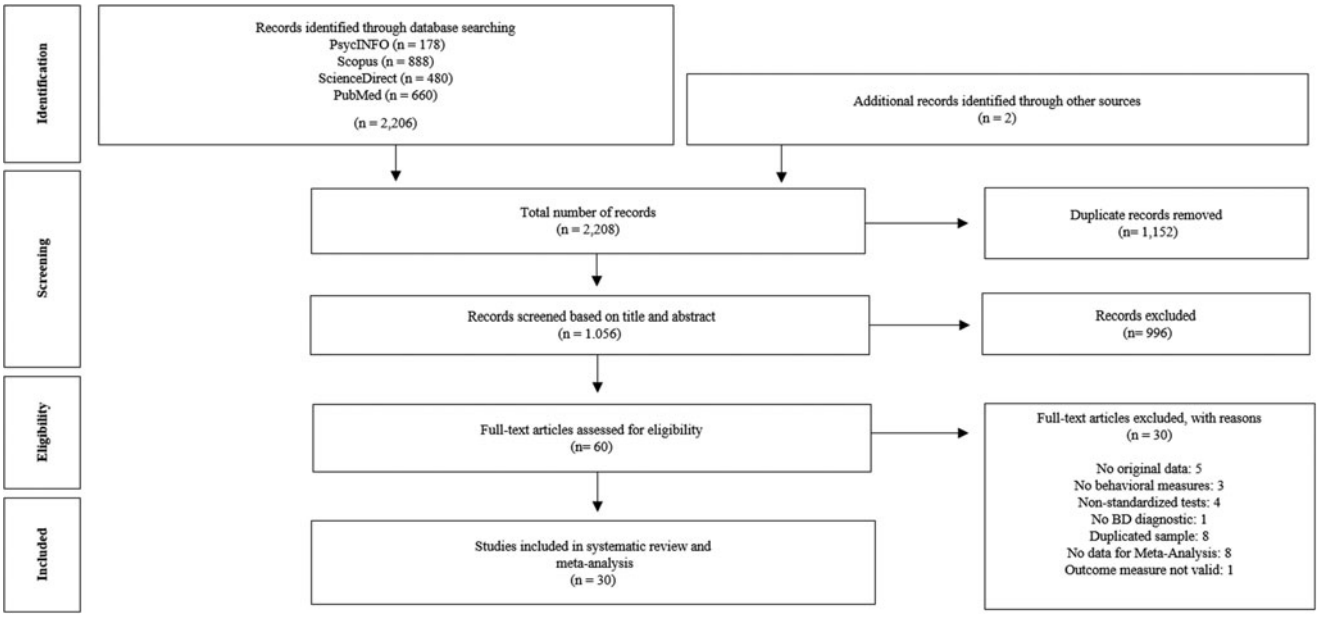


Fig. 1. Study selection flow chart for systematic review and meta-analysis.

excluded were resolved through discussion, with the intervention of two additional authors. In the end, a total of 30 publications were eligible for review and were included in the meta-analysis. The results of the search strategy are summarised in a flow diagram (Fig. 1).

Data extraction and quality assessment

The two researchers independently abstracted the data from the selected articles, collecting the following information: first author, year of publication, sample, mean age of participants, phase of illness, neurocognitive test, neurocognitive outcome, results, age range, gender, study design, neuroimaging test (use of a neuroimaging test during the study), matching of controls, study quality and funding. A description of this information can be found in the supplementary material (online Supplementary Table S2). Article quality was assessed using the Newcastle–Ottawa quality assessment scale (NOS) (Wells et al., 2014). Details of the NOS can be seen in the supplementary material (online Supplementary Table S3).

Statistical analysis

For the meta-analysis, we calculated bias-corrected standardised mean differences (Hedges' g). We analysed the studies in accordance with fixed-effect and random-effects models with the inverse variance method, calculating 95% confidence intervals and *p* values. We analysed heterogeneity by calculating the estimated between-study variance T^2, H and I^2 and the p value using Cochran's Q statistic. We performed separate meta-analyses for decision-making, risk-taking and each construct of impulsivity (response inhibition, delay of gratification and inattention). Stratified analysis was also carried out on phase of illness (euthymia, depression or mania) and diagnosis subtype (BD I or other), where there were at least three studies with these conditions. In addition, we conducted individual task (Balloon Analogue Risk Task and Cambridge Gambling Task) meta-analyses for risk-taking as they are not completely equivalent measures. For domains (decision-making, risk-taking and each construct of impulsivity) with at least ten studies, the risk of publication bias was calculated using funnel plots, Egger's test (Egger, Davey Smith, Schneider, & Minder, 1997) and the rank correlation test (Begg & Mazumdar, 1994). All the analyses were calculated using R version 3.5.1 and the package *Meta* (Schwarzer, Carpenter, & Rücker, 2015).

Results

A total of 30 studies (numbered to improve readability, see Table 1) were included in the meta-analysis. Table 1 summarises the main results and characteristics of the studies included. More information about the studies can be found in the supplementary material (online Supplementary Table S4).

The studies were conducted on adult populations in various countries: USA [2,3,8,9,11,12,24,27,28,30], England [14,22,25], France [15,20], Germany [16,17,26], Brazil [18,21], Argentina [13,19], Italy [4], Canada [6], Egypt [23], Israel [7] and Turkey [10]. Two studies included the populations of more than one country [1,5] and one failed to specify the nationality of its population [29]. Those that specified the particular locus of their study reported that it was carried out in a hospital context; two studies did not provide this information [26,28].

Combined, the studies provided data on 1628 participants with BD, 47 BD-patient relatives and 1319 controls, with an age range of 18–67 years. Among the patients, individuals were either in a euthymic state or remission, a depressive state, a manic or a hypomanic state, or a mixed state. A total of 28 studies were exclusively cross-sectional; the remaining two [16,27] included, in addition to a cross-sectional component, a follow-up component examining a subsample of the study population in an acute illness phase and subsequent remission. Neuroimaging tests were used in 10 of the 30 studies [9,12,13,14,15,16,17,18,20,26].

In terms of the behavioural measures used in the studies: nine used the Iowa Gambling Task [1,5,8,13,14,18,19,21,30]; six used

https://doi.org/10.1017/S0033291720003086 Published online by Cambridge University Press

https://doi.org/10.1017/S0033291720003086 Published online by Cambridge University Press

Table 1. Main results and characteristics of the selected studies

ID-Article	First author, year-publication	Mean age	Sample	Phase of illness	Neurocognitive test	Neurocognitive Outcome	Results
1.	Adida et al. (2011)	39.75	167 BD-I patients	Mania Depression Euthymia	Iowa Gambling Task (IGT)	Decision-making	BD patients showed impaired decision-making.
		38.8	150 Healthy controls				
2.	Ahn et al. (2011)	39.9	22 BD-I patients	Not specified	Delay Discounting Task	Impulsivity (Delay of gratification)	BD patients showed significant differences in impulsivity in comparison with healthy controls. The patients showed steeper discounting rates.
		37.0	30 Healthy controls				
3.	Bauer et al. (2017)	36.63	184 BD patients	Mania Depression Hypomania Mixed episode Euthymia Undetermined	Affective Go/No-Go task (AGN) Cambridge Gambling task (CGT)	Impulsivity (Response inhibition) Impulsivity (Delay of gratification) Decision-making Risk behaviour	The BD patients showed a significantly impaired performance compared to the healthy subjects in response inhibition. The patients made more errors than healthy subjects. In CGT, the BD patients had more delay aversion, reduced quality of decision-making and greater propensity to take risks than the healthy control group.
		34.82	93 Healthy controls				
4.	Bersani, Quartini, Zullo, and Iannitelli (2016)	44.26	30 BD-I patients	Euthymia	Stop Signal Task (SST)	Impulsivity (Response inhibition)	Groups did not differ regarding the response inhibition task.
		42.87	15 Healthy controls				
5.	Brambilla et al. (2013)	44.6	70 BD-I patients	Euthymia	Iowa Gambling Task (IGT)	Decision-making	BD patients showed significantly impaired decision-making in comparison with healthy individuals.
		43.9	140 Healthy controls				
6.	Cheema, MacQueen, and Hassel (2015)	34.8	21 BD-I patients	Euthymia	Emotional Go/No-Go Task	Impulsivity (Response inhibition)	There were no significant differences between groups in emotional Go/No-Go task, although BD patients committed more errors than healthy controls
		30.1	23 Healthy controls				
7.	Duek, Osher, Belmaker, Bersudsky, and Kofman (2014)	42.15	40 BD-I patients	Euthymia	Single Key Impulsivity Paradigm (SKIP)	Impulsivity (Delay of gratification)	There were no differences between BD patients and healthy participants in impulsive behaviour (SKIP task).
		38.89	41 Healthy controls				
8.	Edge et al. (2013)	36.0	55 BD-I patients	Euthymia	Iowa Gambling Task (IGT)	Decision-making	There were no significant differences between BD patients and healthy participants in decision-making (IGT).
		33.5	39 Healthy controls				
9.	Fleck et al. (2011)	32.21	18 BD-I patients	Depression Mixed episode	Go/No-Go Task	Impulsivity (Response inhibition)	The BD group made more commission errors than healthy controls in Go/No-Go task.
		33	10 Healthy controls				
10.	Hidiroğlu et al. (2013)	35.50	30 BD-I patients	Euthymia	Balloon Analogue Risk Task (BART)	Risk behaviour	The BD participants showed higher risk-taking behaviour in the BART with significant lower adjustment scores than healthy participants. No significant differences were found between BD patients and BD-Relatives.
		40.20	25 BD-Relatives				
		35.73	30 Healthy controls				

https://doi.org/10.1017/S0033291720003086 Published online by Cambridge University Press

11.	Holmes et al. (2009)	41.14	55 BD patients	Depression Hypo(mania) Euthymia	Balloon Analogue Risk Task (BART)	Risk behaviour	There were no significant differences between BD patients and healthy subjects on the number of adjusted pumps on the BART. When the BD sample was divided into euthymic, depressed and (hypo)manic subgroups, groups did not differ in performance on the BART.
		38.3	25 Healthy controls				
12.	Hummer et al. (2013)	33.83	74 BD patients	Depression Mania Euthymia	Picture of Facial Affect (Go/No-Go Task)	Impulsivity (Response inhibition)	There were no significant differences between groups for none of the conditions in the affective go/no-go task.
		32	30 Healthy controls				
13.	Ibanez et al. (2012)	40.1	13 BD-II patients	Euthymia	Iowa Gambling Task (IGT)	Decision-making	There were no differences between groups in decision-making.
		35.1	25 Healthy controls				
14.	Jogia, Dima, Kumari, and Frangou (2012)	42.5	36 BD I patients	Euthymia	Iowa Gambling Task (IGT)	Decision-making	There were no statistically significant differences in the outcome measures of the IGT between groups
		37.6	37 Healthy controls				
15.	Kaladjian et al. (2009)	37.9	20 BD-I patients	Euthymia	Go/No-Go Task	Impulsivity (Response inhibition)	Regarding task performance, there were no significant differences in response times and accuracy.
		34.6	20 Healthy controls				
16.	Kopf et al. (2018)	42	36 BD patients	Depression Euthymia	Combined Stop-Signal-Go/ No-Go Task	Impulsivity (Response inhibition)	Depressed BD patients differed significantly from controls in their reaction time, as well as, in their Stop Signal Reaction Time (SSRT). They also made significantly more omissions errors than controls. However, when patients were remitted, they did not differ from controls in reaction time or SSRT. They also decreased to the level of healthy controls in their omission error rate.
		36	15 Follow-up remitted patients				
		42.3	30 Healthy controls				
17.	Linke et al. (2013)	45	19 BD-I patients	Euthymia	Cambridge Gambling Task (CGT)	Risk behaviour	There were significant differences between groups in CGT. BD patients and BD-Relatives committed more errors than healthy participants, but there were no differences between BD and BD-Relatives.
		45	19 Healthy controls				
		28	22 BD-Relatives				
18.	Malloy-Diniz et al. (2011)	41	95 BD patients	Euthymia	Continuous Performance Test (CPT-II) Iowa Gambling Task (IGT)	Impulsivity (Response inhibition) Impulsivity (Inattention) Decision making	Bipolar patients had a significantly worse performance than controls on almost all measures of impulsiveness and decision-making.
		32	94 Healthy controls				
19.	Martino, Strejilevich, Torralva, and Manes (2011)	37.7	48 BD-I patients	Euthymia	Iowa Gambling Task (IGT)	Decision-making	No difference between BD-I or BD-II patients and controls on any of IGT outcome measures.
		42.8	37 BD-II patients				
		40	34 Healthy controls				

(*Continued*)

https://doi.org/10.1017/S0033291720003086 Published online by Cambridge University Press

Table 1. (*Continued.*)

ID-Article	First author, year-publication	Mean age	Sample	Phase of illness	Neurocognitive test	Neurocognitive Outcome	Results
20.	Mazzola-Pomietto, Kaladjian, Azorin, Anton, and Jeanningros (2009)	35.8 34.6	16 BD-I patients 16 Healthy controls	Mania	Go/NoGo Task	Impulsivity (Response inhibition)	Patients and healthy subjects distinguished the Go and No Go stimuli with a similar ease and developed a similar tendency toward responding. However, manic patients had longer response time on Go trials than healthy subjects.
21.	de Moraes et al. (2013)	40.9 31.2	95 BD patients 115 Healthy controls	Euthymia	Continuous Performance Test II (CPT-II) Iowa Gambling Task (IGT)	Impulsivity (Response inhibition) Impulsivity (Inattention) Decision-making	Bipolar patients had a significantly poorer performance on all impulsivity measures and decision-making compared to the control group.
22.	Murphy et al. (2001)	36.3 36.4	18 BD-I patients 26 Healthy controls	Mania	Decision-making task	Decision-making	Manic patients earned fewer points, took longer to make decisions and made optimal choices less often than control subjects.
23.	Okasha et al. (2014)	27 25.7	60 BD patients 30 Healthy controls	Euthymia	Continuous Performance Test (CPT)	Impulsivity (Response inhibition) Impulsivity (Inattention)	Patients with BD had highly significant total errors of commissions (impulsivity) and total errors of omissions (inattention).
24.	Reddy et al. (2014)	44 41.4	68 BD patients (46 BD-I and 22 BD-II) 36 Healthy controls	Mania Depression Euthymia	Balloon Analogue Risk Task (BART)	Risk behaviour	BD patients performed comparably to controls on risk-taking behaviour. However, patients taking antipsychotic drugs had lower scores on the BART.
25.	Rubinsztein, Michael, Underwood, Tempest, and Sahakain (2006)	43.7 39.3	24 BD patients 26 Healthy controls	Depression	Decision-making task	Decision-making	Decision-making was significantly impaired in BD depression. They were slower at making their decisions and made suboptimal choices more often than the healthy group.
26.	Scholz et al. (2016)	44 44	24 BD-I patients 24 Healthy controls	Euthymia	Cambridge Gambling Task (CGT)	Risk behaviour	There was a significant difference in risk-taking behaviour. BD-I patients showed riskier decisions in comparison with the control group.
27.	Strakowski et al. (2010)	29 31	108 BD-I patients 48 Healthy controls	Mania Mixed episode Depression Euthymia	Logan Stop-Signal Task (SST) Delayed reward task (DRT) Degraded stimulus version of the CPT (DSCPT)	Impulsivity (Response inhibition) Impulsivity (Delay of gratification) Impulsivity (Inattention)	Bipolar manic/mixed subjects had elevated impulsivity and differed on all impulsivity measures. The BD subjects had longer stop signal reaction times (SSRTs), more impulsive responses and slower reaction time on the delayed reward task and lower sensitivity (A′) and bias (B″) on the degraded-stimulus CPT. In depression, BD subjects showed more impulsive responding on the DRT but showed no other significant differences on the others tasks. During euthymia, BD subjects had no significant differences from controls on any task.

28.	Swann, Lijffijt, Lane, Steinberg, and Moeller (2009)	36.1	112 BD patients	Mania Depression Euthymia	Immediate Memory Task (IMT) Single Key Impulsivity Paradigm (SKIP)	Impulsivity (Response inhibition) Impulsivity (Delay of gratification)	Response inhibition was impaired in BD and was associated with a more severe course of illness. On IMT, the results showed fewer correct detections and slower reaction times in BD than in controls. Subjects with BD made more SKIP responses than did controls.
		32.8	71 Healthy controls				
29.	Taylor Tavares et al. (2007)	32.6	17 BD-II patients	Depression	Cambridge Gamble Task (CGT)	Decision-making	BD patients did not show impairments in decision-making.
		34.8	25 Healthy controls				
30.	van Enkhuizen et al. (2014)	33.8	16 BD patients	Mania Hypomania	Iowa Gambling Task (IGT)	Decision-making	There was a significant difference in decision-making. BD subjects made less advantageous choices in comparison with healthy controls.
		33.9	17 Healthy controls				

BD, bipolar disorder; BD-I, bipolar disorder type I; BD-II, bipolar disorder type II; BD-R, bipolar disorder relatives; HC, healthy controls; RTs, reaction time; IGT, Iowa Gambling Task; DRT, delayed reward task; DSCPT, degraded stimulus version of the Continuous Performance Test; SST, Stop-Signal Task; IMT, Immediate Memory Task; DMT, Delayed Memory Task; SKIP, Single Key Impulsivity Paradigm; CGT, Cambridge Gamble Task; CPT-II, Continuous Performance Test II.

the Go/No-Go Task in its various forms [3,6,9,12,15,20]; four used the Cambridge Gambling Task [3,17,26,29]; three used the Continuous Performance Test [18,21,23]; three used the Balloon Analogue Risk Task [10,11,24]; two used the Stop Signal Task [4,27]; two used the Single Key Impulsivity Paradigm [7,28]; two used the Decision-making Task [22,25]; and four employed alternative methods, including the Delay Discounting Task [2], the Combined Stop-Signal-Go/No-Go Task [16], the Immediate Memory Task [28], the Delayed reward task and the Degraded stimulus version of the Continuous Performance Test [27]. Online Supplementary Table S5 shows which cognitive domain was measured by each neurocognitive test.

Twenty-two studies were of good methodological quality, having a score equal to or greater than 7 on the Newcastle–Ottawa Scale [1,4,5,6,7,9,10,12,13,14,15,16,17,19,20,22,23,25,26,27,29,30]. The other eight were of medium quality, having a score of 5 or 6 [2,3,8,11,18,21,24,28].

Impulsivity

It is important to note that behavioural measures of impulsivity can be subdivided into those that explore response inhibition, those that explore the ability to delay gratification and those that explore inattention. Some studies evaluated more than one modality of impulsivity at the same time.

Response inhibition

A measure of response inhibition was provided by 13 studies [3,4,6,9,12,15,16,18,20,21,23,27,28]. In six of them [3,9,18,21,23,28], BD patients performed significantly worse than healthy controls did in response inhibition tests, whereas in five studies no significant difference between the groups was found [4,6,12,15,20]. The remaining two studies, however, showed disparate results: in one, the results indicated that BD patients differed significantly from controls when the former was depressed but not when they were in remission [16]; in the other, bipolar manic/mixed subjects differed significantly from healthy subjects on the response inhibition task, but bipolar depressed and euthymic patients did not [27]. There is a moderate risk of bias, as no study had the maximum score of 9 in the quality assessment and four studies (30.8%) were not considered of high quality (score under 7).

In the meta-analysis there was no significant heterogeneity between studies [$\tau^2 = 0.0146$; $H = 1.16$ (1.00–1.62); $I^2 = 26.1\%$ (0.0–61.7%); $Q = 16.24$, $p = 0.180$] and the pooled effect size was 0.49 [fixed-effect model; CI (0.38–0.60); $z = 8.92$; $p < 0.0001$]. There was no evidence of publication bias in the funnel plot (online Supplementary Fig. S1) and Egger's test was not significant ($p = 0.6058$). The effect size in the subgroups were very similar and significant in the separate meta-analyses of euthymic [fixed-effect model; SMD = 0.59; CI (0.43–0.75); $z = 7.23$; $p < 0.0001$], depressed [fixed-effect model; SMD = 0.48; CI (0.16–0.81); $z = 2.92$; $p = 0.0035$] and manic [fixed-effect model; SMD = 0.47; CI (0.21–0.74); $z = 3.49$; $p = 0.0005$] samples, but not significant for the subgroup of the BD I and euthymic sample [fixed-effect model; SMD = 0.29; CI (−0.07 to 0.65); $z = 1.59$; $p = 0.1121$]. More detailed results are shown in the forest plot in Fig. 2. To control possible bias, we also conducted a meta-analysis without the studies that used the Continuous Performance Test as a dependent measure in Inattention. The results were very similar [fixed-effect model; SMD = 0.40; CI (0.26–0.53); $z = 5.84$; $p < 0.0001$]. More information is shown in the forest plot in online Supplementary Fig. S2.

https://doi.org/10.1017/S0033291720003086 Published online by Cambridge University Press

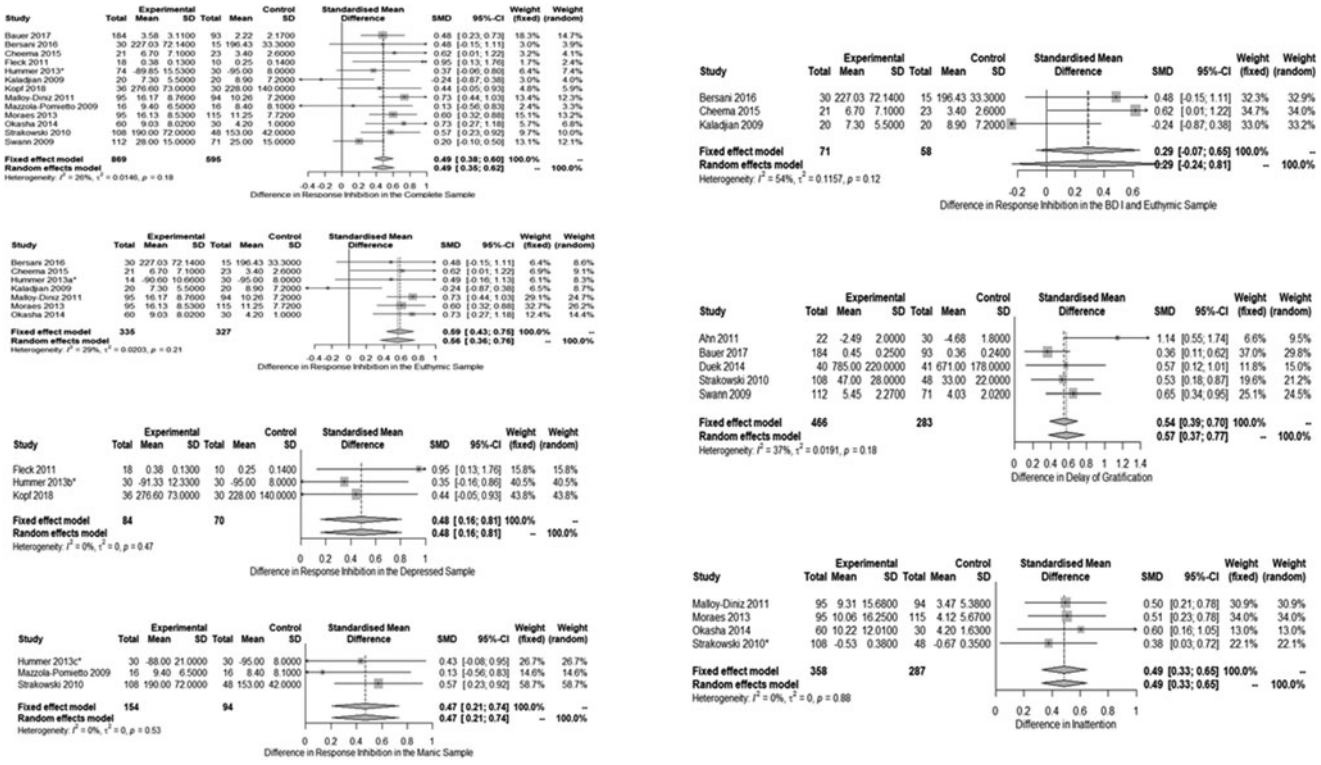


Fig. 2. Forest plots of impulsivity (response inhibition, delay of gratification and inattention) in the total sample and in a subset of euthymic, depressed, manic and bipolar disorder I patients.

Delay of gratification

Five studies evaluated the ability to delay gratification [2,3,7,27,28]. Three of them [2,3,28] found that inability to delay gratification for a larger reward was greater among the BD patients than in the control group. One study found no significant difference between the BD patients in the euthymic phase and the healthy subjects [7]. Other found that BD manic/mixed and depressed patients exhibited more impulsive responding than healthy subjects, but found no such difference between healthy subjects and euthymic patients [27]. The risk of bias was high as three studies (60.0%) were not considered of high quality and no study had the maximum score of 9.

In the meta-analysis there was no heterogeneity between studies [$\tau^2 = 0.0191$; $H = 1.26$ (1.00–2.06); $I^2 = 36.9\%$ (0.0–76.5%); $Q = 6.34$, $p = 0.175$] and the pooled effect size was 0.54 [fixed-effect model; CI (0.39–0.70); z = 6.97; $p < 0.0001$]. More detailed results are shown in Fig. 2.

To control possible bias, we conducted the meta-analysis without the studies that use Cambridge Gambling Task, since it had already been considered in decision-making behaviour. Results were very similar [fixed-effect model; SMD = 0.65; CI (0.46–0.84); $z = 6.60$; $p < 0.0001$]. More information is shown in online Supplementary Fig. S3.

Inattention

Inattention was measured by four studies [18,21,23,27]. Three of them found increases in omission errors in patients with BD compared with healthy subjects [18,21,23]. The remaining study found significant differences in a measure of inattention between BD manic subjects and controls. Nevertheless, no significant differences were found between depressive or euthymic BD patients and healthy subjects [27]. The risk of bias was high as two studies (50.0%) were not considered of high quality and all studies scored under 8.

In the meta-analysis there was no significant heterogeneity between studies [$\tau^2 = 0$; $H = 1.00$ (1.00–1.23); $I^2 = 0.0\%$ (0.0–33.6%); $Q = 0.69$, $p = 0.875$] and the pooled effect size was 0.49 [fixed-effect model; CI (0.33–0.65); $z = 5.92$; $p < 0.0001$]. More detailed results are shown in the forest plot in Fig. 2.

Decision-making

In total, 13 of the 30 studies in this meta-analysis looked specifically at the decision-making of BD patients [1,3,5,8,13,14,18,19,21,22,25,29,30]. Eight studies found significant differences between BD patients and healthy subjects [1,3,5,18,21,24,25,30]. There were no significant differences in decision-making performance in five studies [8,13,14,19,29]. We consider that there exists a moderate risk of bias as no study had the maximum score and four studies (30.8%) were not considered of high quality in the assessment.

In the meta-analysis there was significant heterogeneity between the studies [$\tau^2 = 0.2847$; $H = 2.98$ (2.39–3.70); $I^2 = 88.7\%$ (82.5–92.7%); $Q = 106.26$, $p < 0.0001$] and the pooled effect size was 0.61 [random-effects model; CI (−0.93 to −0.28); $z = -3.68$; $p = 0.0002$]. There was no evidence of publication bias from the funnel plot (online Supplementary Fig. S1) or Egger's test ($p = 0.2454$). In the meta-analysis, the effect size was large but not significant for patients in the depressed phase [random-effects model; SMD = −0.92; CI (−2.99 to 1.15); $z = -0.87$; $p = 0.3828$] and large and significant for patients in the manic phase [random-effects model; SMD = −1.35; CI (−2.43 to

https://doi.org/10.1017/S0033291720003086 Published online by Cambridge University Press

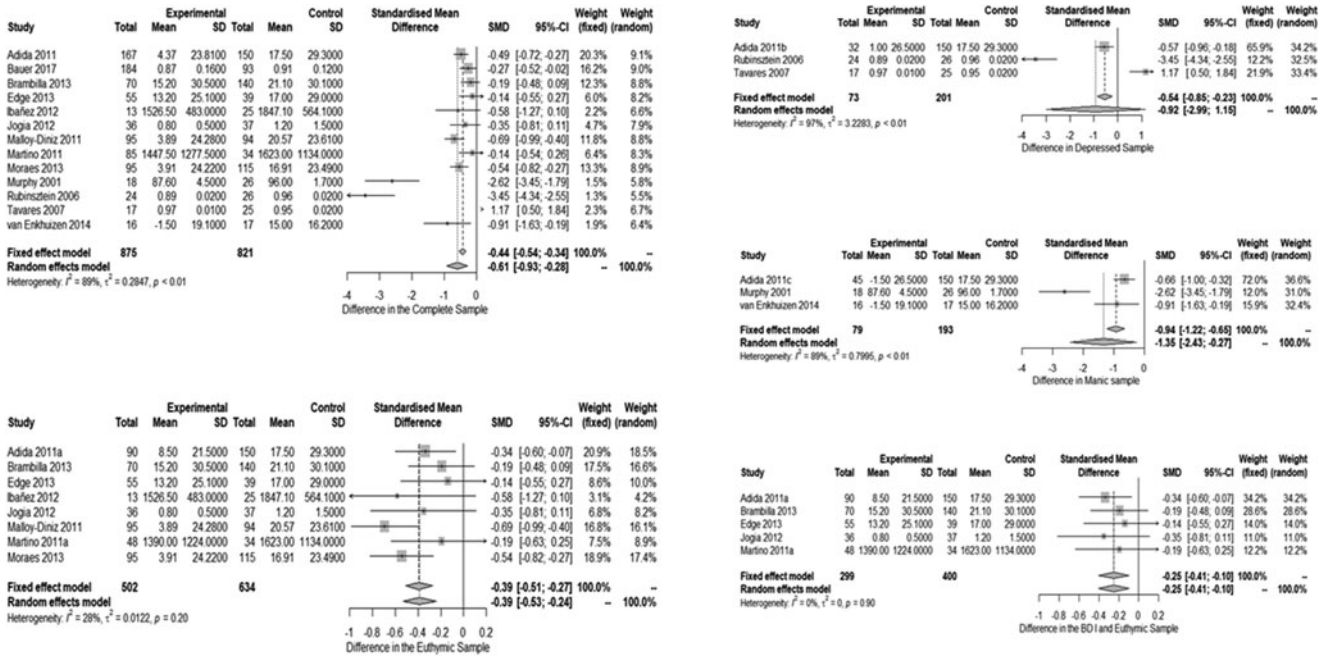


Fig. 3. Forest plots of decision-making in the total sample and in a subset of euthymic, depressed, manic and bipolar disorder I patients.

−0.27); $z = -2.45$; $p = 0.0143$] but with significant heterogeneity between studies and a high risk of publication bias. This is due to the fact that the meta-analysis only included studies with small sample size and there were important differences in effect sizes among them. There was a small but significant effect size for euthymic patients [fixed-effect model; SMD = −0.39; CI (−0.51 to −0.27); $z = -6.39$; $p < 0.0001$] and for the subgroup of BD I and euthymic patients [fixed-effect model; SMD = −0.25; CI (−0.41 to −0.10); $z = -3.22$; $p = 0.0013$]. There was no significant heterogeneity between the studies. More detailed results are shown in the forest plot in Fig. 3.

As the majority of studies used behavioural measure as the Iowa Gambling Task, we conducted a meta-analysis with only those studies and the effect size was lower [fixed-effects model; SMD = −0.43; CI (−0.55 to −0.32); $z = -7.49$; $p < 0.0001$] in comparison with the complete meta-analysis, however, heterogeneity was not significant. Detailed information is shown in online Supplementary Fig. S4.

Risk-taking behaviour

Only six of the 30 studies reported on risk-taking behaviour measures [3,10,11,17,24,26]. Four [3,10,17,26] found significantly lower risk adjustment in BD patients compared with healthy subjects; the other two showed disparate results [11,24]. The risk of bias was high as three studies (50.0%) were not considered of high quality.

In the meta-analysis there was significant heterogeneity between the studies [$\tau^2 = 0.2230$; $H = 2.31$ (1.58–3.39); $I^2 = 81.3\%$ (60.0–91.3%); $Q = 26.75$, $p < 0.0001$] and the pooled effect size was 0.41 [random-effects model; CI (−0.02 to 0.84); $z = 1.88$; $p = 0.0598$] and only marginally significant for the entire sample. However, the effect size was large and statistically significant for the subgroup of BD I and euthymic patients [fixed-effect model; SMD = 0.92; CI (0.57–1.26); $z = 5.24$; $p < 0.0001$] with no significant heterogeneity. More detailed results are shown in the forest plot in Fig. 4.

In individual task meta-analyses, the effect size was very similar and not significant for Balloon Analogue Risk Task [random-effects model; SMD = 0.43; CI (−0.35 to 1.20); $z = 1.08$; $p = 0.2799$] and Cambridge Gambling Task [random-effects model; SMD = 0.41; CI (−0.22 to 1.04); $z = 1.28$; $p = 0.1992$]. More detailed results are shown in the forest plot in the supplementary material (online Supplementary Fig. S2).

A summary of the main results of different meta-analyses is shown in the supplementary material (online Supplementary Table S6).

Discussion

The present study synthesised and contrasted the findings of 30 case-control studies of BD individuals subjected to neuropsychological evaluations of their impulsivity, decision-making and risk-taking behaviour by way of behavioural tests. To the best of our knowledge, this is the first systematic review and meta-analysis that has simultaneously analysed these three cognitive domains in adults with BD considering behavioural measures only. Previous reviews have considered both behavioural measures and questionnaires or self-report measures.

Impulsivity

Looking at the results obtained, impulsivity was higher among BD subjects compared with healthy controls and appear to be present in all phases of the illness. Manic, depressive and euthymic bipolar patients' performance was worse than that of healthy controls on response inhibition. They also showed evidence of impairment in the delay of gratification and poorer performance on inattention tasks; however, there were not enough studies to analyse the subgroups separately here.

Our findings are consistent with those of a previous review suggesting that high impulsivity is a core feature of BD that persists even after manic and depressed symptoms are in remission

https://doi.org/10.1017/S0033291720003086 Published online by Cambridge University Press

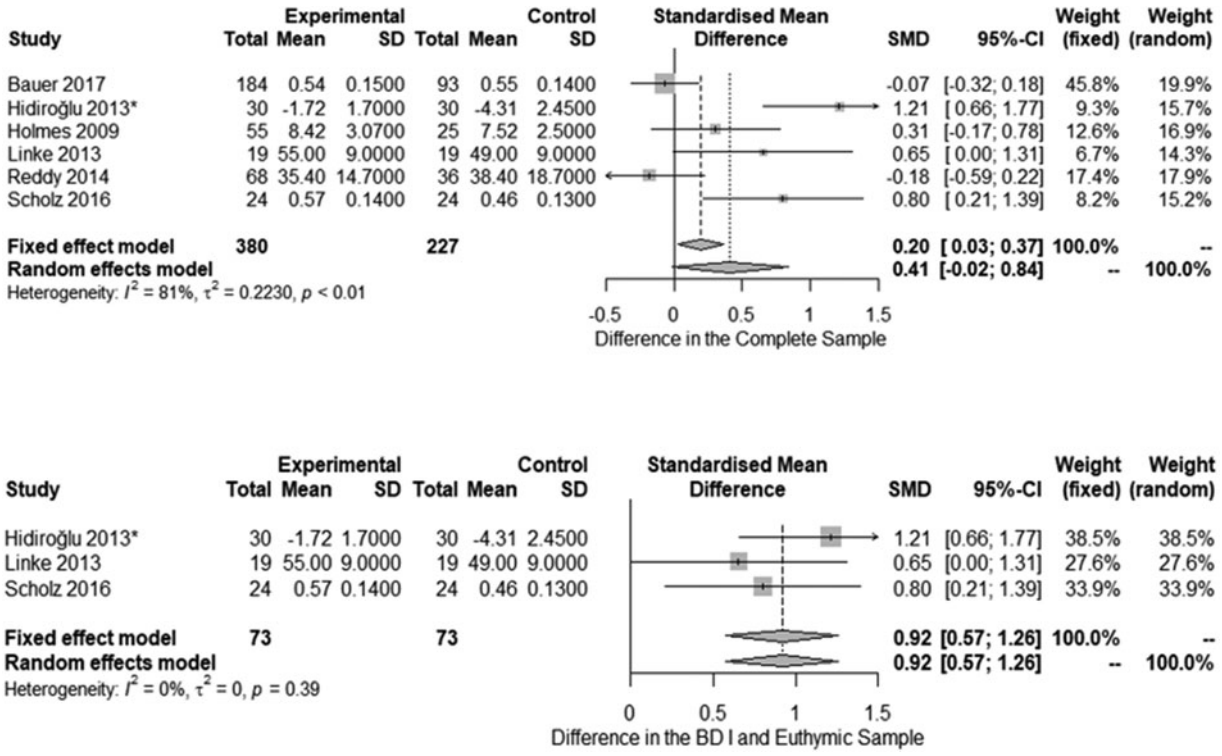


Fig. 4. Forest plots of risk-taking behaviour in the total sample and in a subset of euthymic and bipolar disorder I patients.

(Najt et al., 2007). In contrast, a review carried out by Newman and Meyer (2014) failed to detect significant differences in behavioural manifestations of impulsivity between euthymic BD patients and controls. Their findings did not coincide with those found in our study, maybe, due to the limited number of studies that used behavioural paradigms included in their review and the reduced sample size, as our meta-analysis included three cross-sectional studies [4,6,23] published after Newman and Meyer's (2014) review, as well as a further two that they did not include [12,21].

This same study also reported significant differences in impulsivity between euthymic patients and healthy controls when self-report measures were considered. Indeed, an extensive body of research has observed high impulsivity in BD in all its phases using self-report measures (Henna et al., 2013; Saddichha & Schuetz, 2014). Our results, therefore, support this body of research by extending similar findings to behavioural measures of impulsivity. In summary, impulsivity does appear to be affected in adult BD subjects in all phases of the disorder, suggesting that impulsive behaviour in BD is relatively independent of mood state.

Decision-making

Our meta-analyses results suggest a deficit in decision-making in BD, and the necessity to analyse if the impairment in decision-making has a state-dependent component. The differences found in decision-making were mainly related to the number of correct decisions made by subjects. Our results suggest that individuals diagnosed with BD make optimal choices significantly less often than healthy controls.

We found high heterogeneity between studies when we included the entire sample and the subgroup with symptoms of mania, indicating that the studies were not comparable and, together with the moderately risk of bias, suggested that the results should be interpreted with caution.

In manic and depressive phases, the performance of BD subjects tended to be worse than that of healthy controls with large size effect [22, 25], although for the depression phase this difference was not significant and for the manic phase heterogeneity was significant and the risk of publication bias was high. With respect to the euthymic phase, our results indicated here too that the performance of BD patients was worse but with small effect size than that of healthy controls. Nevertheless, this finding was not significant in the studies conducted by Samamé et al. (2012) and Edge et al. (2013). This divergence in euthymic phase results might be explained by the fact that our meta-analysis included four studies published after the meta-analyses by Samamé et al. (2012) and Edge et al. (2013). Finally, our findings are consistent with a recent analysis suggesting the existence of different cognitive profiles of decision-making in patients diagnosed with BD (Jiménez et al., 2018). Future studies should attempt to answer the question whether the heterogeneity in the results is influenced by the role of other variables, such as medication and comorbidity with other psychiatric disorders.

Risk-taking behaviour

Our meta-analysis results indicated that there are no significant differences between BD subjects and healthy controls in terms of risk-taking behaviour. A similar pattern of findings was obtained in stratified analysis for individual tasks (Balloon Analogue Risk Task and Cambridge Gambling Task). Nevertheless, these findings should be interpreted with caution as the studies included were few, showed high heterogeneity and there was a high risk of bias. This could explain the fact that the result of the meta-analysis reached only marginal significance

https://doi.org/10.1017/S0033291720003086 Published online by Cambridge University Press

in the comparison between BD individuals and controls, even though four of the six studies included indicated that subjects with BD had a lower risk adjustment than that of controls [3,10,17,28]. In addition, our meta-analysis showed significant differences in risk-taking when we compared the euthymic BD I group with the control group, indicating that the euthymic group was more likely to become involved in behaviours that could lead to danger or loss. To the best of our knowledge, no other systematic reviews or meta-analyses have examined this issue. Hence, our results should be considered preliminary. The profile of risk-taking impairment in BD remains to be determined until more data become available.

Limitations

Our study findings should be understood in light of its limitations. First, certain studies may have been excluded because they did not report the necessary results to allow their inclusion in the meta-analysis. Second, considerable heterogeneity was found across the studies on decision-making and risk-taking behaviour. In particular, the type and number of measures used to assess decision-making and risky behaviour varied considerably between studies. There was a lack of consensus on which neuropsychological tasks should be used to assess each cognitive domain, and the same task could be used to measure various domains since performance on most tests involved more than one cognitive process. The use of multiple outcome measures from the same task could increase bias. Heterogeneity was also reflected in the samples. Some studies included a BD I sample while others used a sample made up of BD II subjects. As for BD phases, the study samples comprised patients in different mood states (mania, depression, hypomania, mixed episode or euthymia). In an attempt to overcome this limitation, we carried out a stratified analysis based on the phase of illness (euthymia, depression or mania), an analysis based on diagnosed subtype (BD type I or other) and analysis based on the task used in decision-making (Iowa Gambling Task) and risk-taking behaviour (Balloon Analogue Risk Task or Cambridge Gambling Task). Furthermore, we used recommended methods (e.g. random-effects models) for accounting the observed heterogeneity. Third, a perusal of the effect sizes suggests that some studies may have had insufficient power to detect significant group differences. In a similar vein, the possibility of publication bias is always a concern because studies with null results are less likely than those reporting positive associations to be published. Funnel plots and Egger's test results did not suggest reporting bias on response inhibition and decision-making; but, unfortunately, publication bias could not be assessed for risk-taking, delay of gratification and inattention, as well as in the different stratified meta-analysis because the number of eligible studies with available data was <10. Lastly, there was a lack of information about variables which can interfere in the performance of subjects. Most studies did not report information regarding medical treatment used and addiction comorbidity (including substance and alcohol use).

Conclusions

The results of the study suggest that behavioural impulsivity is elevated in adults with BD in all phases of the disorder, representing a core and clinically relevant feature of BD that persists beyond mood symptoms. Decision-making also appears to be altered in BD, but heterogeneity across the studies was high. Finally, risk-taking behaviour appears to be affected in BD I and euthymic individuals; however, these findings should be viewed as preliminary, as very few studies have formally evaluated the risk-taking in BD patients and the heterogeneity between those, we did examine was high. To exclude biases resulting from high heterogeneity, the homogenisation of neuropsychological measures remains a challenge for the future. Future research should also determine which tasks are better at measuring core aspects of impulsivity, decision-making and risk-taking behaviour. In addition, our results underscore the need for longitudinal studies with larger samples that can provide more accurate results.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S0033291720003086.

Acknowledgements. Fermin Mayoral Cleries and Jose Guzman-Parra have received funding from the Andalusia Government in the grants for human resources reinforcement in the research activity (*Acción A de intesificación 2017* and *Acción B de refuerzos de larga duración 2014*). The authors declare no conflict of interest.

References

Adida, M., Jollant, F., Clark, L., Besnier, N., Guillaume, S., Kaladjian, A., … Courtet, P. (2011). Trait-related decision-making impairment in the three phases of bipolar disorder. *Biological Psychiatry*, *70*(4), 357–365. https://doi.org/10.1016/j.biopsych.2011.01.018.

Ahn, W. Y., Rass, O., Fridberg, D. J., Bishara, A. J., Forsyth, J. K., Breier, A., … O'Donnell, B. F. (2011). Temporal discounting of rewards in patients with bipolar disorder and schizophrenia. *Journal of Abnormal Psychology*, *120*(4), 911–921. https://doi.org/10.1037/a0023333.

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*, *22*(4), 298–314. https://doi.org/10.1080/13546805.2017.1324951.

Bechara, A. (2005). Decision making, impulse control and loss of willpower to resist drugs: A neurocognitive perspective. *Nature Neuroscience*, *8*(11), 1458–1463. https://doi.org/10.1038/nn1584.

Begg, C. B., & Mazumdar, M. (1994). Operating characteristics of a rank correlation test for publication bias. *Biometrics*, *50*(4), 1088–1101.

Bersani, G., Quartini, A., Zullo, D., & Iannitelli, A. (2016). Potential neuroprotective effect of lithium in bipolar patients evaluated by neuropsychological assessment: Preliminary results. *Human Psychopharmacology: Clinical and Experimental*, *31*(1), 19–28. https://doi.org/10.1002/hup.2510.

Brambilla, P., Perlini, C., Bellani, M., Tomelleri, L., Ferro, A., Cerruti, S., … Frangou, S. (2013). Increased salience of gains versus decreased associative learning differentiate bipolar disorder from schizophrenia during incentive decision making. *Psychological Medicine*, *43*(3), 571–580. https://doi.org/10.1017/S0033291712001304.

Chamorro, J., Bernardi, S., Potenza, M., Grant, J., Marsh, R., Wang, S., & Blanco, C. (2012). Impulsivity in the general population: A national study. *Journal of Psychiatric Research*., *46*(8), 994–1001. https://doi.org/10.1016/j.jpsychires.2012.04.023.Impulsivity.

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*(5), 424–437. https://doi.org/10.1080/13546805.2015.1076722.

Christodoulou, T., Lewis, M., Ploubidis, G. B., & Frangou, S. (2006). The relationship of impulsivity to response inhibition and decision-making in remitted patients with bipolar disorder. *European Psychiatry*, *21*(4), 270–273. https://doi.org/10.1016/j.eurpsy.2006.04.006.

de Moraes, P. H. P., Neves, F. S., Vasconcelos, A. G., Lima, I. M. M., Brancaglion, M., Sedyiama, C. Y., … Malloy-Diniz, L. F. (2013). Relationship between neuropsychological and clinical aspects and suicide

https://doi.org/10.1017/S0033291720003086 Published online by Cambridge University Press

attempts in euthymic bipolar patients. *Psicologia: Reflexão e Crítica*, *26*(1), 160–167. https://doi.org/10.1590/S0102-79722013000100017.

Duek, O., Osher, Y., Belmaker, R. H., Bersudsky, Y., & Kofman, O. (2014). Reward sensitivity and anger in euthymic bipolar disorder. *Psychiatry Research*, *215*(1), 95–100. https://doi.org/10.1016/j.psychres.2013.10.028.

Edge, M. D., Johnson, S. L., Ng, T., & Carver, C. S. (2013). Iowa gambling task performance in euthymic bipolar I disorder: A meta-analysis and empirical study. *Journal of Affective Disorders*, *150*(1), 115–122. https://doi.org/10.1016/j.jad.2012.11.027.

Egger, M., Davey Smith, G., Schneider, M., & Minder, C. (1997). Bias in meta-analysis detected by a simple, graphical test. *BMJ* (*Clinical Research Ed.*), *315*(7109), 629–634. https://doi.org/10.1136/bmj.315.7109.629.

Fleck, D. E., Kotwal, R., Eliassen, J. C., Lamy, M., Delbello, M. P., Adler, C. M., … Strakowski, S. M. (2011). Preliminary evidence for increased frontosubcortical activation on a motor impulsivity task in mixed episode bipolar disorder. *Journal of Affective Disorders*, *133*(1–2), 333–339. https://doi.org/10.1016/j.jad.2011.03.053.

Grande, I., Berk, M., Birmaher, B., & Vieta, E. (2016). Bipolar disorder. *The Lancet*, *387*(10027), 1561–1572. https://doi.org/10.1016/S0140-6736(15)00241-X.

Henna, E., Hatch, J. P., Nicoletti, M., Swann, A. C., Zunta-Soares, G., & Soares, J. C. (2013). Is impulsivity a common trait in bipolar and unipolar disorders? *Bipolar Disorders*, *15*(2), 223–227. https://doi.org/10.1111/bdi.12034.

Hidiroğlu, C., Demirci Esen, Ö., Tunca, Z., Neslihan Gârz Yalçin, Ş., Lombardo, L., Glahn, D. C., & Özerdem, A. (2013). Can risk-taking be an endophenotype for bipolar disorder? A study on patients with bipolar disorder type I and their first-degree relatives. *Journal of the International Neuropsychological Society*, *19*(4), 474–482. https://doi.org/10.1017/S1355617713000015.

Holmes, M. K., Bearden, C. E., Barguil, M., Fonseca, M., Monkul, E. S., Nery, F. G., … Glahn, D. C. (2009). Conceptualizing impulsivity and risk taking in bipolar disorder: Importance of history of alcohol abuse. *Bipolar Disorders*, *11*(1), 33–40. https://doi.org/10.1111/j.1399-5618.2008.00657.x.

Hummer, T. A., Hulvershorn, L. A., Karne, H. S., Gunn, A. D., Wang, Y., & Anand, A. (2013). Emotional response inhibition in bipolar disorder: A functional magnetic resonance imaging study of trait- and state-related abnormalities. *Biological Psychiatry*, *73*(2), 136–143. https://doi.org/10.1016/j.biopsych.2012.06.036.

Ibanez, A., Cetkovich, M., Petroni, A., Urquina, H., Baez, S., Gonzalez-Gadea, M. L., … Manes, F. (2012). The neural basis of decision-making and reward processing in adults with euthymic bipolar disorder or attention-deficit/hyperactivity disorder (ADHD). *PLoS ONE*, *7*(5), e37306. https://doi.org/10.1371/journal.pone.0037306.

Jiménez, E., Solé, B., Arias, B., Mitjans, M., Varo, C., Reinares, M., … Benabarre, A. (2018). Characterizing decision-making and reward processing in bipolar disorder: A cluster analysis. *European Neuropsychopharmacology*, *28*(7), 863–874. https://doi.org/10.1016/j.euroneuro.2018.04.001.

Jogia, J., Dima, D., Kumari, V., & Frangou, S. (2012). Frontopolar cortical inefficiency may underpin reward and working memory dysfunction in bipolar disorder. *The World Journal of Biological Psychiatry*, *13*(8), 605–615. https://doi.org/10.3109/15622975.2011.585662.

Kaladjian, A., Jeanningros, R., Azorin, J. M., Nazarian, B., Roth, M., & Mazzola-Pomietto, P. (2009). Reduced brain activation in euthymic bipolar patients during response inhibition: An event-related fMRI study. *Psychiatry Research – Neuroimaging*, *173*(1), 45–51. https://doi.org/10.1016/j.pscychresns.2008.08.003.

Ketter, T. A. (2010). Diagnostic features, prevalence, and impact of bipolar disorder. *The Journal of Clinical Psychiatry*, *71*(06), e14. https://doi.org/10.4088/jcp.8125tx11c.

Kopf, J., Glöckner, S., Schecklmann, M., Dresler, T., Plichta, M. M., Veeh, J., … Reif, A. (2018). Neural correlates of response inhibition in patients with bipolar disorder during acute versus remitted phase. *World Journal of Biological Psychiatry*, *20*(8), 637–646. https://doi.org/10.1080/15622975.2018.1428356.

Leigh, B. C. (1999). Peril, chance, adventure: Concepts of risk, alcohol use and risky behavior in young adults. *Addiction*, *94*(3), 371–383. https://doi.org/10.1046/j.1360-0443.1999.9433717.x.

Linke, J., King, A. V, Poupon, C., Hennerici, M. G., Gass, A., & Wessa, M. (2013). Impaired anatomical connectivity and related executive functions: Differentiating vulnerability and disease marker in bipolar disorder. *Biological Psychiatry*, *74*(12), 908–916. https://doi.org/10.1016/j.biopsych.2013.04.010.

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*(1–2), 221–226. https://doi.org/10.1016/j.jad.2011.03.051.

Martino, D. J., Strejilevich, S. A., Torralva, T., & Manes, F. (2011). Decision making in euthymic bipolar I and bipolar II disorders. *Psychological Medicine*, *41*(6), 1319–1327. https://doi.org/10.1017/S0033291710001832.

Mazzola-Pomietto, P., Kaladjian, A., Azorin, J. M., Anton, J. L., & Jeanningros, R. (2009). Bilateral decrease in ventrolateral prefrontal cortex activation during motor response inhibition in mania. *Journal of Psychiatric Research*, *43*(4), 432–441. https://doi.org/10.1016/j.jpsychires.2008.05.004.

Merikangas, K. R., Jin, R., He, J. P., Kessler, R. C., Lee, S., Sampson, N. A., … Zarkov, Z. (2011). Prevalence and correlates of bipolar spectrum disorder in the World Mental Health Survey Initiative. *Archives of General Psychiatry*, *68*(3), 241–251. https://doi.org/10.1001/archgenpsychiatry.2011.12.

Miskowiak, K. W., Burdick, K. E., Martinez-Aran, A., Bonnin, C. M., Bowie, C. R., Carvalho, A. F., … Vieta, E. (2017). Methodological recommendations for cognition trials in bipolar disorder by the International Society for Bipolar Disorders Targeting Cognition Task Force. *Bipolar Disorders*, *19*(8), 614–626. https://doi.org/10.1111/bdi.12534.

Moeller, F. G., Barratt, E. S., Dougherty, D. M., Schmitz, J. M., & Swann, A. C. (2001). Psychiatric aspects of impulsivity. *American Journal of Psychiatry*, *158*(11), 1783–1793. https://doi.org/10.1176/appi.ajp.158.11.1783.

Moher, D., Liberati, A., Tetzlaff, J., & Altman, D. G. (2009). Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *Annals of Internal Medicine*, *151*(4), 264. https://doi.org/10.7326/0003-4819-151-4-200908180-00135.

Murphy, F. C., Rubinsztein, J. S., Michael, A., Rogers, R. D., Robbins, T. W., Paykel, E. S., & Sahakian, B. J. (2001). Decision-making cognition in mania and depression. *Psychological Medicine*, *31*(4), 679–693. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11352370.

Najt, P., Perez, J., Sanches, M., Peluso, M. A. M., Glahn, D., & Soares, J. C. (2007). Impulsivity and bipolar disorder. *European Neuropsychopharmacology*, *17*(5), 313–320. https://doi.org/10.1016/j.euroneuro.2006.10.002.

Newman, A. L., & Meyer, T. D. (2014). Impulsivity: Present during euthymia in bipolar disorder? – A systematic review. *International Journal of Bipolar Disorders*, *2*(1), 2. https://doi.org/10.1186/2194-7511-2-2.

Okasha, T. A., El Sheikh, M. M., El Missiry, A. A., El Missiry, M. A., El Serafi, D., El Kholy, S., & Abdel Aziz, K. (2014). Cognitive functions in euthymic Egyptian patients with bipolar disorder: Are they different from healthy controls? *Journal of Affective Disorders*, *166*, 14–21. https://doi.org/10.1016/j.jad.2014.04.051.

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*(8), 876–884. https://doi.org/10.1111/bdi.12124.

Reddy, L. F., Lee, J., Davis, M. C., Altshuler, L., Glahn, D. C., Miklowitz, D. J., & Green, M. F. (2014). Impulsivity and risk taking in bipolar disorder and schizophrenia. *Neuropsychopharmacology*, *39*(2), 456–463. https://doi.org/10.1038/npp.2013.218.

Roiser, J., Farmer, A., Lam, D., Burke, A., O'Neill, N., Keating, S., … McGuffin, P. (2009). The effect of positive mood induction on emotional processing in euthymic individuals with bipolar disorder and controls. *Psychological Medicine*, *39*(5), 785–791. https://doi.org/10.1017/S0033291708004200.

Rubinsztein, J. S., Michael, A., Underwood, B. R., Tempest, M., & Sahakain, B. J. (2006). Impaired cognition and decision-making in bipolar depression but no "affective bias" evident. *Psychological Medicine*, *36*(5), 629–639. https://doi.org/10.1017/S0033291705006689.

Saddichha, S., & Schuetz, C. (2014). Is impulsivity in remitted bipolar disorder a stable trait? A meta-analytic review. *Comprehensive Psychiatry*, *55*(7), 1479–1484. https://doi.org/10.1016/j.comppsych.2014.05.010.

Samamé, C., Martino, D. J., & Strejilevich, S. A. (2012). Social cognition in euthymic bipolar disorder: Systematic review and meta-analytic approach.

https://doi.org/10.1017/S0033291720003086 Published online by Cambridge University Press

Acta Psychiatrica Scandinavica, *125*(4), 266–280. https://doi.org/10.1111/j.1600-0447.2011.01808.x.

Scholz, V., Houenou, J., Kollmann, B., Duclap, D., Poupon, C., & Wessa, M. (2016). Dysfunctional decision-making related to white matter alterations in bipolar i disorder. *Journal of Affective Disorders*, *194*, 72–79. https://doi.org/10.1016/j.jad.2015.12.019.

Schwarzer, G., Carpenter, J. R., & Rücker, G. (2015). *Meta-Analysis with R*. Cham: Springer International Publishing. https://doi.org/10.1007/978-3-319-21416-0.

Strakowski, S. M., Fleck, D. E., Delbello, M. P., Adler, C. M., Shear, P. K., Mcelroy, S. L., … Arndt, S. (2009). Characterizing impulsivity in mania. *Bipolar Disorders*, *11*(1), 41–51. https://doi.org/10.1111/j.1399-5618.2008.00658.x.

Strakowski, S. M., Fleck, D. E., Delbello, M. P., Caleb, M., Shear, P. K., Kotwal, R., & Arndt, S. (2010). Impulsivity across the course of bipolar disorder. *Bipolar Disorder*, *12*(3), 285–297. https://doi.org/10.1111/j.1399-5618.2010.00806.x.Impulsivity.

Swann, A. C., Lijffijt, M., Lane, S. D., Steinberg, J. L., & Moeller, F. G. (2009). Severity of bipolar disorder is associated with impairment of response inhibition. *Journal of Affective Disorders*, *116*(1–2), 30–36. https://doi.org/10.1016/j.jad.2008.10.022.

Taylor Tavares, J. V., Clark, L., Cannon, D. M., Erickson, K., Drevets, W. C., & Sahakian, B. J. (2007). Distinct profiles of neurocognitive function in unmedicated unipolar depression and bipolar II depression. *Biological Psychiatry*, *62*(8), 917–924. https://doi.org/10.1016/j.biopsych.2007.05.034.

van Enkhuizen, J., Henry, B. L., Minassian, A., Perry, W., Milienne-Petiot, M., Higa, K. K., … Young, J. W. (2014). Reduced dopamine transporter functioning induces high-reward risk-preference consistent with bipolar disorder. *Neuropsychopharmacology*, *39*(13), 3112–3122. https://doi.org/10.1038/npp.2014.170.

Wells, G. A., Shea, B., Connell, D., Peterson, J., Welch, V., Losos, M., & Tugwell, P. (2014). The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Retrieved from http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp.

Wilson, M. J., & Vassileva, J. (2018). Decision-making under risk, but not under ambiguity, predicts pathological gambling in discrete types of abstinent substance users. *Frontiers in Psychiatry*, *9*, 1–10. https://doi.org/10.3389/fpsyt.2018.00239.

Wright, L., Lipszyc, J., Dupuis, A., Thayapararajah, S. W., & Schachar, R. (2014). Response inhibition and psychopathology: A meta-analysis of Go/No-Go task performance. *Journal of Abnormal Psychology*, *123*(2), 429–439. https://doi.org/10.1037/a0036295.

https://doi.org/10.1017/S0033291720003086 Published online by Cambridge University Press