Psychosocial Recovery-Oriented Treatments in Bipolar Disorders

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11.1   Psychosocial Functioning in Bipolar Disorder

Bipolar disorder (BD) is a mood disorder characterized by recurrent episodes of mania, hypomania, and depression separated by periods of euthymia affecting around 2.4% of the global population [1]. As a lifelong and recurrent illness, BD is associated with functional decline, cognitive impairment, and a reduction in quality of life (QoL) [2–4]. Psychosocial functioning is an essential component of a person's quality of life and includes social, psychological, and occupational domains. In 2001, a landmark review found that between 30 and 60% of adults with BD had significant impairments in occupational and social functioning during periods of euthymia [5]. A possible explanation for pervasive psychosocial dysfunction may be the illness itself or the high prevalence of comorbid mental disorders in BD [6].

Mental health comorbidities in BD are more likely to be multiple than singular, with the World Mental Health Survey reporting a 62% lifetime prevalence of 3 or more comorbidities when strict Diagnostic and Statistical Manual of Mental

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Disorders-IV (DSM-IV) criteria were applied [1]. However, research into the psychosocial effects of multiple comorbidities in BD is limited, often due to lack of power in subgroup analyses [7]. Bennett et al. (2019) [8] published recently the first report that has demonstrated the negative impact of comorbid anxiety disorders and ADHD on psychosocial functioning in BD.

Earlier age at onset of BD is consistently linked with poorer clinical outcomes, including rapid cycling, greater number of mood episodes, and increased risk of suicide [9]. Some studies have linked psychosocial dysfunction with an early onset (<18 years), although this finding is not consistent [10]. The studies that have focused on patients with an early onset suggest that psychosocial impairment is due to earlier disruption in the development of interpersonal skills needed to build and maintain healthy relationships as patients grow older [11]. However, while younger age of onset is associated with an adverse course of illness in adulthood [9], how these may be related to psychosocial functioning has received little attention.

Given the complexity of this illness and its consequences, researchers and clinicians are not only focused on clinical remission but also functional recovery and, more lately, well-being too [12]. This emergent paradigm includes not only symptom recovery but also return to normal functioning and attainment of a meaningful life. In fact, in 1988, Dion and colleagues [13] already pointed out that factors other than symptoms were related to functioning of patients with BD and that treatment should target symptom amelioration as well as reduce a patient's disability [13]. It is known that even after the first manic episode, only 1 out of 3 patients regains psychosocial functioning at 1-year follow-up [14], suggesting that functional outcomes in BD are undoubtedly impaired from the very beginning and should become a priority in therapeutic interventions. Research into BD has often overlooked the role of psychosocial functioning; however, in the last decade, many efforts have been made to improve functioning and well-being in BD.

11.2   Defining and Measuring Psychosocial Functioning

Despite the importance of psychosocial functioning in BD there is not a clear consensus regarding its definition. In the Task Force for the International Society for Bipolar Disorders conducted by Tohen and colleagues in 2009 [15], different definitions of psychosocial functioning were examined but without reaching a consensus. The experts highlighted the definition provided by the International Classification of Functioning, Disability and Health (ICF) in which functioning comprises three different components: body structures and functions; activities and participation; and personal environmental factors. Moreover, the authors of these guidelines underlined that this construct was complex to measure and that besides the ICF, the Functioning Assessment Short Thest (FAST) scale [16] might also constitute a good approach to measure functioning [15]. Before these guidelines, there were other attempts to define psychosocial functioning. For instance, in 2000, Zarate

and colleagues [17] suggested the assessment of psychosocial functioning should involve different behavioral domains such as the individuals' ability to function socially or occupationally, to live independently, and to engage in a romantic life, with functional recovery typically being defined as the restoration of normal role functioning in the domains under scrutiny [17]. This definition represented a breakthrough in the field because in that moment, psychosocial functioning was measured by means of the Global Assessment Functioning Scale (GAF), endorsed by several consecutive editions of the Diagnostic and Statistical Manual of Mental Disorders (DSM). GAF scale provides 1 single score without differentiating between the behavioral domains pointed by Zarate and colleagues [17]. Despite all, the GAF is still the most commonly used clinician rating scale to measure disability, at least in the United States [18]. In 2007, Rosa and colleagues [16] developed a tool to measure functioning, the already mentioned FAST scale. It was specifically created to measure the most common difficulties experienced by patients with BD. The rationale behind this scale is in line with the definition of functioning proposed by Zarate and colleagues in 2000 [17], mostly focused on the assessment of different behavioral domains. More specifically, the FAST targets the following areas: autonomy, occupational and cognitive functioning, financial issues, interpersonal functioning, and leisure time. In this regard, the FAST represented several advantages over the GAF, mainly that it assesses different behavioral domains, it does not rate the symptomatology, and it is specific for BD.

Currently, the DSM-5 no longer encourages the use of the GAF. Instead, the use of the World Health Organization Disability Assessment Schedule 2.0 (WHODAS 2.0) [19] is recommended. The WHODAS 2.0 allows the assessment of functioning and disability irrespective of diagnosis; that is, it can reflect difficulties due to any medical or psychiatric illness. In contrast, both the GAF and the FAST are limited to the impact of the psychiatric disease on functioning, excluding the medical or environmental limitations. The GAF, FAST, WHODAS 2.0, or ICF core sets specific for BD [20, 21] are clinical tools, either rater administered (GAF, FAST, ICF core sets) or self-administered (WHODAS 2.0), but other approaches exist. For instance, the UCSD Performance-based skills Assessment (UPSA) [22] is based on task performance and measures functional capacity, assessing the skills involved in community tasks such as comprehension and planning, finance, communication, mobility, and house management. Figure 11.1 represents an overview of some different scales available to measure functioning in BD during the last 40 years, starting in 1980, when the GAF was first endorsed by the DSM-III until the present.

The scales presented in Fig. 11.1 are just a little part of the big picture of the measurement of psychosocial functioning in BD. Nevertheless, it fairly represents the great variability that exists. It is likely that the way the researcher or clinician defines psychosocial functioning will determine the tool to measure it, but the reverse is true as well: the use of one tool or another implies how the concept of psychosocial functioning is understood. To overcome this bias, it would be ideal that psychosocial functioning could be measured taking into account three different perspectives: (1) a subjective view using a self-administered scale, such as the Sheehan

YEAR	SCALE/Measurement
1980	DSM-III starts endorsing FAST
2000	LIFE-RIFT (to assess functioning in affective disorders) (Leon et al, 2000)
2001	UPSA (Petterson et al, 2000)
2007	• FAST scale (Rosa et al, 2007) • ICF score tests for BD (Vieta et al, 2007) • Validation of the MSFI for BD (Bernset al, 2007)
2009	Validation of the SDS for BD (Arbuckle et al, 2009)
2013	DSM-5 starts endorsing WHODAS 2.0 and do not recommend the use of GAF anymore
2021	A measurement of functioning combining three perspectives is recommended: • A subjective assessment (using a self-administered scale) • A semi-objective assessment (using interviewer-rated scales) • An objective assessment using performance-based tools

Fig. 11.1 Chronology of Functioning measures

Disability Scale for BD (SDS) [23] or the WHODAS 2.0; (2) a semi-objective scale, using the FAST, GAF, or LIFE-RIFT [24], which are interviewer rated based on patients' answers; and finally (3) an objective scale, like the UPSA, which is performance based and measures functional capacity. Combining these three different approaches might help to disentangle all the variables associated with functional impairment observed in BD.

11.3   Variables Related with Psychosocial Functioning

Many variables have been associated with functional outcome in BD, including demographic, clinical, and neurocognitive factors.

Concerning the sociodemographic factors, it seems that male patients [25, 26] as well as older patients [26] show poorer functional outcomes. On the other hand, being married could represent a protective factor against functional impairment [27, 28]. Higher socioeconomic status, based on education and employment, has also been associated with better functional outcomes [28, 29].

Regarding the clinical variables, the presence of subsyndromal depressive symptoms has been consistently reported as the strongest factor associated with functional impairment [2, 25, 30–35]. Other clinical variables include history of psychosis, episode density, poor sleep quality, and longer illness duration [33, 34, 36–39]. Psychiatric comorbidity, particularly with substance use disorder (e.g., cannabis, alcohol) and personality disorders, can also negatively influence functional outcomes in patients with BD [40–44].

Finally, regarding neurocognitive variables, the evidence suggests that there are three or four discrete and coherent profiles, one cognitively intact and comparable to the general population, plus one or two subgroups presenting with selective moderate impairments, and a globally impaired subgroup with severe impairments across cognitive domains. Similar findings have been reported from studies with

cross-diagnostic samples involving people with different diagnoses across the psychosis spectrum [45].

Verbal memory has been found to be a good predictor of functional outcome in several studies [10, 35, 46–48]. However, variables related to other neurocognitive areas have also been reported, including executive functions, processing speed, and attention [28, 49, 50]. It might be hypothesized that the neurocognitive variables influencing functional outcome in BD may vary depending on illness progression. For instance, patients in early stages of the disease seem to present a more selective profile of cognitive impairment, with some domains capable of improving 1 year after the first manic episode, including improvements in processing speed and executive functions [51]. In this line, at least two studies have found that first-episode patients who did not relapse during 1-year follow-up could improve their neurocognitive functioning [52, 53]; hence, preserving neurocognition from the very beginning of the illness might guarantee better functional outcomes.

11.4   Restoring Psychosocial Functioning

11.4.1 Pharmacological Interventions

Research on pharmacological and nonpharmacological treatments to restore functioning in BD is still immature. As previously mentioned, the link between functional outcomes and neurocognition is well recognized, which is why in recent years many efforts have improved cognition, including both pharmacological and psychological treatments. In fact, new trends in pharmacological treatments include focusing on restoring cognitive functioning rather than psychosocial functioning. Among the most promising medical treatments to improve cognition in BD are mifepristone [54], lurasidone [55], and erythropoietin, this last according to different studies improves verbal memory and learning in mood disorders [56, 57]. Given the link between neurocognition and psychosocial functioning, it is likely that the efforts directed to improve neurocognition will also improve functional outcome; however, so far, no studies on pharmacological treatments have addressed both issues at the same time. It is worth mentioning that the methodological recommendations for cognition trials by the Cognition Task Force from the International Society for Bipolar Disorders encourage the inclusion of a functional measure as a key secondary outcome [58]. In this regard, a tool to measure functional improvement that allows the researchers and clinicians to classify patients into different categories of functional performance could be useful to assess the efficacy of these treatments [59]. A very promising antidepressant is vortioxetine, a structural novel medication, which may have therapeutic effects on cognition. In a recent study, vortioxetine both as monotherapy and as adjunctive treatment performed better than SSRI monotherapy in improving psychosocial outcomes. Since functional assessments represent a broader construct, reflecting at the same time patients' symptomatic as well as their cognitive status, these improvements highlight a broad effect of vortioxetine across symptoms domains [60].

11.4.2 Psychological Interventions

In contrast to the area of pharmacological treatments, in the field of psychological interventions several efforts have been made lately to design therapies to restore psychosocial functioning in BD. Cognitive interventions have emerged as a new treatment option to promote functional recovery of patients with BD. The association between cognition and function has been extensively explored, with most evidence suggesting significant contributions of cognitive impairment to reduced functional capacities. The first attempt was an open trial using a program named Cognitive Rehabilitation [61]. The authors included a total of 18 patients with sub-syndromal depressive symptoms and after 14 sessions of cognitive rehabilitation, patients improved cognitive performance and functional outcome. More interestingly, the findings showed that changes in executive function accounted, in part, for the improvements in occupational functioning. The first randomized controlled trial (RCT) implementing a similar therapy was conducted in 2013 by Torrent and colleagues [62]. The efficacy of functional remediation (FR) was proved in terms of improving functional outcomes in euthymic patients with moderate to severe functional impairment at baseline. Moreover, improvement in psychosocial functioning was maintained after 6 months' follow-up [63]. However, the impact of the intervention was low in terms of cognition. Contrary to other therapies labeled as "cognitive remediation," FR is specially centered on functional recovery, focusing on the training of neurocognitive skills that are useful for daily functioning. Hence, this approach might be suitable especially for patients in late stages of the illness and who present moderate to severe functional impairment. Currently, this approach has been adapted and being validated in other populations such as first-episode patients to assess its impact on psychosocial functioning as main outcome likewise in other measures such as neurocognition, depressive symptoms, psychological well-being, and cognitive complaints in order to become a tool that could diminish the impact that the new diagnosis has in patient's lives after the onset of psychosis, reducing sick leave and academic absenteeism improving their productivity and alleviating the academic and/or work difficulties they often experience.

Another preliminary study conducted in the Netherlands included 12 patients and replicated the positive results in functional outcome after receiving a shorter FR program [64]. However, not all the interventions targeting cognitive rehabilitation were found to improve functional outcome. For instance, another RCT conducted by Demant and colleagues (2015) [65] found no improvement on either cognition or functional outcome after a 12-week intervention. It is worth mentioning that these negative results might be explained by some methodological limitations of the trial, including the length of the intervention (too short) or the fact that patients were subsyndromic at study enrolment. Another study leaded by Lewandowski and colleagues (2017) [66] assessed the efficacy of an internet-based cognitive remediation program in patients with BD compared with an active control group both in neurocognition and community functioning. After treatment, patients who received the internet-based program improved cognitive performance in processing speed,

visual learning and memory domains, and the composite score. These results were maintained over 6 months after finishing the intervention; however, the intervention was not associated with change in community functioning, although cognitive variation was associated with functional change across the sample.

Another program called action-based cognitive remediation (ABCR) is a manual-based restorative cognitive remediation program. The treatment duration is about 10 weeks with 2-h sessions twice a week. Each participant met with a therapist for a goal setting before the first session. The treatment includes computerized training, cognitive strategies together with practical activities to enable to transfer cognitive skills to everyday life. The sessions cover meta-cognition, visual and verbal working memory, attention, memory, and executive functions. In the first study investigating the effect of this program vs control treatment in patients with remitted BD, ABCR did not had a significant effect on the primary outcome, speed of complex cognitive processing. Nevertheless, there was an effect of ACBR vs control treatment on the secondary outcome, an executive functions measure of planning skills at treatment completion. Among the tertiary outcomes, there was an improvement on subjective functioning, and measures of verbal memory and spatial working [67].

In a naturalistic, open label non-controlled study the authors found that in patients with BD the global functioning improved by computerized working memory remediation, which was assessed by the FAST scale [68, 69]. In contrast, in a randomized clinical trial 39 patients with BD were randomized to either treatment as usual (TAU) or Cognitive Behavior Rehabilitation (CBR), an add-on treatment delivered in 12 weekly group sessions; the CBR intervention showed promising results in improving some of the commonly impaired cognitive domains without changes in functional and QoL scores. A longer follow-up may be necessary to detect chances in these domains [70].

A proof-of-concept, single-blind randomized trial recruited participants aged 18–65 with BD not currently experiencing an episode. Participants were assigned to receive Cognitive Remediation Therapy (CRT) in addition to treatment as usual (TAU) or TAU alone following completion of the baseline assessment. The four main feasibility outcomes were considered primary with equal weighting: trial feasibility, CRT intervention acceptability, cognitive outcomes, and functional outcomes. Despite a relatively small sample size ($N = 60$), large effects on cognition (working memory and executive functions), functioning, and goal attainment were observed, enduring for 3 months after the end of therapy. These results indicate high feasibility and acceptability of individual, therapist-led CRT using the established CIRCuiTS program, as a potential treatment to enhance cognition and functioning for BD. CIRCuiTS therapy was delivered using a combination of session types for all participants comprising: face-to-face and telephone sessions and practice together with independent practice sessions with computerized system [71].

It is difficult to measure the power of these current approaches in changing functioning, since very few studies have used psychosocial functioning as a primary outcome. The results of the first systematic review of the possible moderating effect

of stage of illness on the impact of psychosocial treatments on functional outcomes in established BD suggest that psychosocial interventions are more effective for targeting general or social functioning in the earlier than later stage of BD [72]. In this line, in a multicenter, randomized, controlled trial patients at clinical risk for a serious mental illness presenting subthreshold bipolar symptoms with already impaired psychosocial functioning benefit from early group sessions of cognitive behavioral psychotherapy (CBT) [73]. Furthermore, two studies have been designed to examine the effectiveness of group psychotherapy on global adaptative function and neuropsychological functioning in early-stage bipolar disorder [74] and in young people at increased risk for developing a BD [75]; the results are expected in the near future.

11.5 Preventing Functional Decline

So far, there is no strong evidence regarding the prevention of functional decline in BD. The following section includes some targets and treatments that could address this issue and deserve to be further explored.

11.5.1 Addressing Subthreshold Depressive Symptoms

Between 20 and 50% of patients suffer inter-episodically or chronic residual depressive symptoms depending on the definition applied [76]. Subsyndromal depression interferes with role functioning in essential domains of normal life, such as work, duties at home, and maintaining relationships. In this regard, subthreshold depressive symptoms together with neurocognitive impairment might be one of the strongest predictors of functional outcome [2, 33, 35, 47, 77, 78]. However, the relationship between functional outcome and subthreshold depressive symptoms might not be linear and unidirectional; instead, they seem to influence one another [79]. Besides the implications in functional outcome, residual depressive symptoms are also a major cause of relapse [80, 81], consequently affecting psychosocial functioning and QoL [2]. The treatment of residual depressive symptoms during euthymia is an unmet need, but fortunately, clinical research has begun to investigate how to tackle them. One recent RCT proved that adjunctive extended-release quetiapine at a dose of 300 mg daily was significantly more effective than placebo in the treatment of subthreshold depressive symptoms [82], but no significant improvement was detected in functional outcome. One possible explanation is that the sample size was not powered enough to detect significant changes in this secondary outcome.

Regarding psychological interventions, a limited number of therapies have addressed subthreshold depressive symptoms as a primary outcome. To the best of our knowledge, only one pilot RCT study assessed the effect of Eye Movement Desensitization and Reprocessing therapy on this type of symptomatology. Specifically, patients in the treatment group showed a statistically significant

improvement in depressive and hypomanic symptoms when compared with treatment as usual at 12-month follow-up; however, psychosocial functioning was not assessed [83]. Another multicenter study of Eye Movement Desensitization and Reprocessing with a bigger sample is underway with the objective to reduce symptoms and relapses and improve psychosocial functioning [84]. Regarding FR, secondary analyses showed that patients with subsyndromal symptoms could also improve psychosocial functioning after the therapy [85].

Other therapies include an approach testing the long-term efficacy of an intervention that combined cognitive behavior therapy (CBT) and psychoeducation, which has also been described to be effective in terms of symptoms and social-occupational functioning improvement [86]. Positive results in social functioning were also found with CBT [87]. Inder and colleagues (2015) [88] randomized a group of patients with BD to Interpersonal and Social Rhythm Therapy or specialist supportive care, and both groups improved in depressive/manic symptoms and social functioning. Finally, an intensive psychotherapy (family-focused treatment [FFT], Interpersonal and Social Rhythm Therapy (IPSRT), or CBT) in patients with BD during an acute depressive episode also showed beneficial functional outcomes [89]. The IPSRT Therapy contributes to reduce the levels of anxiety by helping patients to address their interpersonal deficits and improving their emotional dysregulation, and not just by managing affective symptoms. As expected, at the follow-up we observed an improvement of GAF score. This result emphasizes the importance of the interpersonal intervention in improving all aspects of patients' life, thus contributing to prevent mood shifts [90]. Another recent study shows that participants with recurrent mood disorders described improved functioning related to therapies that formulate their mood disorder in terms of a model, such as IPSRT with or without cognitive remediation. This supports the person in undertaking practical routines that can be integrated into daily life, focuses on communication and problem-solving skills, and engenders a sense of hope by working with the person to develop self-management strategies relevant to their specific symptom experiences [91].

Finally, positive results have also been reported on anxious and depressive symptoms using mindfulness-based cognitive therapy [92–94].

Although more research is needed, it might be hypothesized that treating subthreshold depressive symptoms could be an indirect pathway to improve psychosocial functioning.

11.5.2 Enhancing Cognitive Reserve

Cognitive reserve (CR) is the capacity of the adult brain to endure neuropathology, minimizing clinical manifestations and allowing a successful accomplishment of cognitive tasks [95]. Genetics determine, to some extent, CR; however, environmental factors such as an active lifestyle, education, and brain stimulation (mental activities) can also influence it. In BD the most common ways to measure CR include years of education, premorbid Intelligence Quotient, and leisure activities.

So far, no interventions have tested whether improving CR enhances functioning, but some studies suggest that CR is a good predictor of both cognitive and psychosocial outcome in euthymic patients with BD [96, 97]. In a recent publication, the findings show that CR may be protective against cognitive impairment in both BD and major depressive disorder, and these effects were observed in euthymia and during depressive episodes of varying severity. These findings highlight the importance of investigating such variables in the neuropsychological evaluation of mood disorders, which may help to understand the cognitive heterogeneity within these populations [98]. Further, it could also play an important role in patients with first psychotic episode since CR has shown to predict psychosocial functioning 2 years after the first episode [99]. Hence, given the role of CR both in chronic patients and at early stages, this might constitute an area to explore and enhance to prevent functional decline [100]. In this regard, there is another ongoing trial by de la Serna et al. (2021) [101] that aims to enhance CR in child, adolescent, and young adult offspring of patients diagnosed with schizophrenia or BD; however, so far, no preliminary results are available.

In a study assessing cognitive impairment across four cognitive domains in 80 participants, the results show that individuals with cognitively impaired profiles demonstrate more cognitive decline after illness onset. Cognitive reserve may be one of the factors underlying cognitive variability across people with bipolar disorder. Patients in the intermediate and severe subgroups may be in greater need of interventions targeting cognitive difficulties [45].

11.5.3 Diet and Physical Exercise

"Nutritional Psychiatry" is an emerging area of research that has great potential as an adjunctive tool for the prevention and treatment of diverse neuropsychiatric disorders. Several nutrition-related aspects, such as obesity, dietary patterns, gut microbiome composition and gut permeability, bioactive food compounds, and nutrients can influence pathways implicated in the pathophysiology of mood disorders. A dietary pattern is composed of multiple nutrients and bioactive compounds that can theoretically modulate pathways associated with mood disorders. The Mediterranean diet, generally characterized by a higher intake of fruits, vegetables, legumes, nuts, whole grains, and good quality sources of protein (i.e., fish and/or seafood), have demonstrated benefits in cognitive performance and decreased risk of psychiatric disorders [102].

People with mood disorders have shown higher ratios of unhealthy lifestyle choices, including poor diet quality and suboptimal nutrition. Diet and nutrition impact on brain/mental health, but cognitive outcomes have been less researched in psychiatric disorders. Neurocognitive dysfunction is a major driver of social dysfunction and a therapeutic target in mood disorders, although effective cognitive-enhancers are currently lacking [103].

Obesity can also impact cognitive functioning [104] and, in turn, cognitive impairment could be a predictor of weight gain [105]. Hence, it seems that weight

increase and cognitive impairment can influence one another. Moreover, another study has found that increased body mass index (BMI) was associated with a more chronic course of the disease, longer duration of illness, and lower psychosocial functioning [106]. In line with this, Bond and colleagues (2010) [107] found that those patients who suffered a clinically significant weight gain (defined as gaining ≥7% of baseline weight over 12 months) had significantly poorer functional outcomes at 12-month follow-up, and, interestingly, functional impairment was independent from current mood symptoms.

Poor dietary habits and a sedentary lifestyle can increase physical and psychiatric morbidity, worsen psychosocial and cognitive functioning, and predict a poor pharmacological response. That is why clinicians treating individuals with BD face a dual challenge of treating not only patients' brains but also their bodies. Interventions targeting healthy habits (including nutrition and exercise) are expected to benefit patients with BD. One RCT examined the effects of a 20-week CBT intervention (NEW tx) for BD consisting of 3 modules: nutrition, exercise, and wellness [108]; patients who underwent the treatment showed improvements in nutritional habits, exercise, depressive symptoms, and overall functioning. Hence, this study provides preliminary evidence that improving nutrition and promoting an active lifestyle is associated with functional improvement and mood symptoms in patients with BD. Another previous study showed the efficacy of an intervention on healthy lifestyle, nutrition, and physical exercise on muscle mass index, particularly in women [109]. These lifestyle interventions are promising since they demonstrate that people with BD can engage and be successful in these types of therapies. Therapeutic mechanisms of action are still unknown but might include different pathways, for example, by reducing morbidity (i.e., depressive symptoms), which in turn would improve functional outcome [110], or by enhancing treatment effects, including the synergistic effects of exercise in combination with other treatments. For instance, in schizophrenia there is some preliminary evidence suggesting that cognitive remediation efficacy can be enhanced by aerobic exercise-induced BDNF upregulation [111, 112].

11.5.4 Multicomponent Programs

One advantage of this type of intervention is to tackle different areas to be improved at the same time, hence allowing a holistic treatment of patients, taking into account not only education on the illness but also how to improve healthy lifestyles and functional outcomes. Following the premise that no single psychosocial intervention might be sufficient to address the morbidity, the functional impairment and the consequences associated with severe mental illnesses [113], multicomponent programs, and care packages are being developed for patients with BD.

An example of this kind of treatment that has proven to be effective in BD is the Integrated Risk Reduction Intervention developed by Frank and colleagues (2015) [114]. More specifically, this program consists of 17 sessions grouped in different modules, including psychoeducation, training to improve sleep/wake patterns and social rhythm regularity, nutrition, physical activity, and healthy habits (smoking

cessation). Results from this study showed that patients who followed the intervention significantly reduce their BMI. Moreover, 3 variables (C-reactive protein, total cholesterol, and instability of total sleep time) contributed to a combined moderator of faster decrease in BMI with Integrated Risk Reduction Intervention treatment.

Recently, the Bipolar Disorder and Depression Unit in Barcelona has developed an integrative approach consisting of therapeutic components of broader programs that the Barcelona Bipolar Disorders Program had previously developed and whose effectiveness had been proven separately, such as psychoeducation for patients [115], psychoeducation for family members [116], and FR [117]. In addition, an important emphasis is given to the promotion of a healthy lifestyle, and a module focused on mindfulness-based cognitive therapy has also been included. Therefore, some contents of psychoeducation for patients have been combined with a session for family members and complemented with aspects related to health promotion, mindfulness training, and strategies for cognitive and functional enhancement, always as adjunctive to pharmacological treatment. This integrative approach combines the main components of different treatments to cover broader therapeutic objectives, to improve the prognosis of the disease in both clinical and functional aspects, as well as the well-being and QoL of those who suffer from BD [118]. Due to the characteristics of the intervention (12 sessions of 90 min each), in case it shows its efficacy, it could be easily implemented in routine clinical care.

11.6   Personal Recovery: Well-Being and QoL

Subjective assessments and patient-reported outcomes are gaining ground in the field of BD [119, 120]. As in psychosocial functioning, the problem with subjective measures is the variability in the definitions and in the instruments to assess the subjective experience of these patients [119]. It is common that terms such as QoL, well-being, or life satisfaction are used as synonyms and interchangeable terms [119]. Moreover, the current lack of consensus between these construct definitions add uncertainty and complication to select an appropriate instrument to measure this dimension. Despite all, the subjective experience should always be taken into account since it can also impact on the course of the illness. Some studies indicate that the improvement in well-being provides a protective effect against recurrence [121], and it has also been found that low levels in QoL are associated with an increase in oxidative stress [122]. For this reason, it is important not only to evaluate objective outcomes (symptoms and functioning) but also to assess patients' subjective experience, since they can provide valuable information and might be an essential part to ensure better outcomes in BD.

11.6.1 Pharmacological Interventions

Rajagopalan et al. (2016) [123] tested the effects of lurasidone as monotherapy or as adjunctive to lithium/valproate on health-related QoL (HRQoL). They found

that patients in both conditions increased HRQoL. However, this improvement was not independent of changes in depression, indicating that the effect of lurasidone on improving patient HRQoL may act through a reduction in depressive symptoms associated with BD. Similarly, Gonda and colleagues (2016) [124] found that patients enhanced both their work functional outcome and QoL after receiving prophylactic lamotrigine therapy at 6 months follow-up. In young patients (10–17 years old) with an acute episode of bipolar depression, it was found that those who received olanzapine/fluoxetine combination presented better QoL scores compared with those receiving placebo [125].

11.6.2 Psychological Interventions

Even though physical activity is not a psychological intervention itself, it is well known for increasing well-being and QoL; however, the impact of this kind of interventions has been less studied in the field of BD. Vancampfort and colleagues (2017) [126] proved the effect of 150 min/week of physical activity on physical, psychological, social, and environmental QoL; those patients who did not meet the established minimum (150 min) showed lower QoL outcomes.

Involving the family, O'Donnell and colleagues (2017) [127] tested the effect of 2 psychological interventions on QoL scores in a sample of adolescents with BD. They compared the efficacy of a FFT plus pharmacotherapy vs brief psychoeducation plus pharmacotherapy on self-related QoL over 2 years. They found the 2 groups did not differ in overall QoL scores at 24 months follow-up. However, adolescents who received the FFT had greater improvements in quality of family relationships and physical well-being compared with the brief psychoeducation program. Besides, internet-based approaches using smartphones are gaining traction [128, 129], a useful and attractive tool especially for the young population with BD [130]. So far, some preliminary studies using a mobile application (SIMPLe) have reported an improvement of biological rhythms [131] and increased QoL and well-being [129]. An important finding is that patients with BD and mild cognitive deficits do not present any limitation in using mental health apps [132].

There is much room for improvement in the field of subjective well-being and QoL. These abovementioned interventions may shed some light regarding the path to follow. Nevertheless, it is important to keep in mind that those patients who suffer from more depressive symptoms, irritability, and psychiatric comorbid conditions present lower QoL and functional outcomes [133, 134]; hence, all the strategies directed to reduce medical and psychiatric burdens might also be useful to increase patients' well-being and QoL. It is also worth mentioning that some authors defend that QoL not only depends on clinical remission but also relies on functional recovery [12]. In this line, poor QoL is also associated with poor occupational outcome, reduced academic attainment [135], and difficulties in activities of daily life [136]. Future studies should include subjective measures (such as QoL, well-being) to better understand the relationship with these clinical variables. Figure 11.2 represents a brief summary of the main interventions targeting cognition and functioning.

Intervention	Delivery method	Setting	Duration	Core therapy components
Compensatory cognitive remediation (Deckersbach et al, 2010)	Non-computerized training	Individual	50 min . Total 14 sessions	Training of cognitive skills with adaptative level of difficulty. Strategy learning focused on daily life management. Mood monitoring
Personalized restorative remediation (Preiss et al, 2013)	Computerized (CogniFit)	Individual	30 min three times per week for 8 weeks. Total 24 session	Traiing personalized bawsed on baseline evaluation. Cognitive tasks with adaptative level of difficulty.
Functional remediation (Torrent et al, 2013)	Pen-and-paper tasks and group activities	Group	90 min weekly for 21 weeks Total: 21 sessions	Education on cognitive deficits and training on strategies to manage cognitive difficulties.
Compensatory cognitive remediation (Demant et al, 2015)	Computerized (RehabCom)	Group	120 min weekly sessions for 3 months. Total 12 sessions	Psychoeducation and awareness of cognitive deficits. Computer practising and training of adaptative and compensatory strategies.
Functional remediation (Zyto et al, 2016)	Non-computerized individual training and group activities	Individual&Group	90 min weekly for 6 weeks & 45 min weekly for 6 weeks Total: 12 sessions	Personalized goal setting and strategy learning to cope with cognitive difficulties.
Neuroplasticity informed cognitive remediation (Lewandowsky et al, 2017)	CompuJterized (BrainWorks)	Individual	45 min three times per week for 6 mponths (70 sessions)	Computer practising with games of adaptative difficulty level based on user performance. Bottom-up training
Compensatory cognitive remediation (Veeh et al, 2017)	Computerized (HappyNeuron Pro)	Individual&Group	90 minuts weekly for three months (12 sessions)	Computer tasks with adaptative difficulty level.
ABSR (Ott et al, 2020)	Combination (computerized and cognitive strategies)	Individual&Group	10 weeks with 2 hours session twice a week	Computerized training, cognitive strategies and practical activities to enable the transfer of cognitive skills to everyday life.
CIRCuiTS (Strawbridge et al, 2020)	Combination Computerized (Circuits program) and face-to-face, telephone and drop in sessions	Individual	3 sessions per week, target total 20-30 hours	Fundamental restorative cognitive processes and compensatory metacognitive skills.

Fig. 11.2 Main interventions targeting cognition and functioning in bipolar disorder

11.7 Conclusions

Different findings highlight that improvement in functioning depends on a set of influential factors that start with cognition. Neuropsychological assessment may help specify individual prognoses. Improving cognitive impairment for BD would alleviate long-term functional disability [137]. Regardless of the great variability in the assessment of psychosocial functioning, many efforts have successfully improved functional outcomes in BD. Currently, the interventions that have proven to be effective at enhancing functioning and/or QoL include lurasidone, lamotrigine, FR, some programs of cognitive remediation, ISPRT, and FFT, among others. These therapies have set the stage for developing further interventions to prevent functional decline and ensure well-being, because this is where we go. Ideally, future therapies should focus not only on restoring functional outcomes but also preventing functional decline and enhancing QoL and well-being. In this regard, those programs that target cognitive enhancement and promote healthy lifestyles (including healthy nutrition patterns and physical activity) are urgently needed, since they constitute a preventive tool for cognitive and functional decline. Although more studies are still needed, multicomponent therapies might be also a good option since they include different approaches to cover several areas at a time (symptoms, functioning, cognition, well-being, etc.). Finally, it is likely that the future will also include personalized treatments focusing on tailored interventions that may differ from one patient to another [138]; in this sense, the type and duration of interventions might differ from patients recently diagnosed, patients with a complex course of the illness and population at risk to develop a psychiatric disorder.

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