

# Premorbid Cognitive Dysfunction and Endophenotypes in Bipolar Disorder: A Rapid Review



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## ABSTRACT

On the contrary that happened with schizophrenia, it has not been completely clarify if cognitive alterations precede the illness or are a consequence of it. Although some data indicate that some cognitive deficits are already present before the illness begins, more studies are still needed.

**Keywords:** Bipolar; Cognitive; Familar; Endophenotype

## Introduction

The poor existing evidence about these aspect indicated that premorbid bipolars patients did not show significant cognitive execution differences versus controls but they did versus premorbid schizophrenics [1] (even thought, these subjects were evaluated by a cognitive battery designed more for military purposes than clinical). Other studies have shown similar data, noting that, in contrast to other pathologies, severe premorbid cognitive dysfunction is not a dominant feature in bipolar disorder [2]. In general, these data would indicate that, if there is a premorbid cognitive malfunction, this would be mild or moderate. Other studies show that the severity of cognitive deficits in high-risk youth for bipolar disorder was relatively less pronounced compared to high-risk youth for schizophrenia, except for psychomotor speed, sustained attention and some executive aspects such as those based on the interference Stroop tests. Unlike schizophrenia, deficits in planning and working memory are not considered as factors of cognitive vulnerability. The severity of the deficit in verbal memory was relatively modest in young people with high risk for bipolarity compared to those of schizophrenia [3]. Another new meta-analysis by Bora et al. [4] on young family members at high risk for bipolar disorder (from 10 to 25 years old) composed of 18 studies (786 descendants and siblings of bipolar patients and 794 healthy controls) display modest

cognitive deficits in several domains: processing speed, sustained attention, visual and verbal memory, and, unlike in schizophrenia, they also do not affect the areas of executive functioning as well as it do not show alterations in working memory whose execution was not different from the control group Bora et al. [4] recognize several limitations in their meta-analysis.

The same transversal nature of the study, the lack of relevant information (such as subliminal manic symptoms or the use of substances and medications), the heterogeneity of cognitive impairment intensity of bipolar disorder and the inability to study specific cognitive domains due to the small number of available studies. Even thought, it is interesting to highlight that they are studies which suggests a short portion of bipolar patients presents a very severe cognitive disorder [5,6]. Developmental cognitive deficits in bipolars might be only evident in a subgroup with pronounced cognitive disrepair and in first degree familiar of them (opposite to other patients and familiars, whom abilities might be intact). In the study carried out by Serna et al. [7], the cognition of children and adolescents' descendants of patients diagnosed with bipolar disorder or schizophrenia was analyzed versus control subjects. Both groups of children with diagnosed relatives showed poorer performance in some cognitive areas compared to controls.

Some of these cognitive difficulties (visual memory) were common to both groups of descendants, while others were specific to each group, such as verbal learning and working memory in children of parents with schizophrenia and the Processing Speed Index (test of perception and visual organization, visual exploration and hand-eye coordination) for the ones with bipolar patients.

In this sense, they exposed that the cognitive difficulties in visual memory shown by both groups of descendants could point to a common endophenotype for the two disorders. Along investigations that have included unaffected relatives, it seems that they present, at lower degree, learning difficulties and verbal memory [170] Martínez Arán et al. [8]. The study carried out by Gourovitch et al. [9] on the cognitive domains in seven pairs of discordant monozygotic twins in bipolar disease and seven pairs of monozygotic twins without pathology. The data showed that the affected twins were significantly altered (compared to the unaffected twins and the ones without pathology) in some measures of visuospatial function and some measures of verbal memory. The unaffected twins had significantly worse performance than the sane controls in memory tasks (Brown-Peterson tasks were used in this study), in verbal learning and in the Wechsler memory coefficient. Even so, the cognitive deficiencies observed in the bipolar twins were much milder than those found in samples of discordant monozygotic twins for schizophrenia.

Other meta-analyses found evidence of moderate deficits in executive functions and verbal memory in first-degree relatives of bipolar patients Arts et al. [10-11]. A further meta-analysis by Bora et al. [12], comparing neurocognition in first-degree relatives of patients with schizophrenia and bipolar disorder, showed that the cognition of relatives with bipolar disorder was significantly altered in processing speed and verbal fluency. In general, both groups saw their processing speed significantly altered, but the performance of bipolar relatives was intermediate between that of the relatives of schizophrenia and healthy controls, not only in speed but in all domains (although there were no significant differences between both groups of relatives in visual memory and sustained attention). Given all the data presented on cognitive endophenotypes, it can be understood that exists a genetic component for bipolar disorder, as in schizophrenic disorder, although the influences of environmental factors cannot be denied. So it would not be impossible to make changes in the psychosocial environment of the patients in order to improve, not only its symptomatology, but also its social and work adjustment [13-14].

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