

TO BE OR NOT TO BE...

BIPOLAR DISORDER IN CHILDREN?

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Introduction.

- Throughout these past years, we have been observing as clinicians, like a sort of “fascination”, patients, parents and teachers to identify bipolar disorders in “*difficult children and adolescents*”.

On several occasions, “to be bipolar” was experienced by the patients as a kind of identification with a group. Conversely, “not being bipolar” was expressed as anger, sadness, lack of understanding from the treating team, instead of relief.

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- Whether or not it is possible to diagnose paediatric mania in the spectrum of bipolar affective disorder is controversial.
- One thing is for sure, bipolar disorder is probably misdiagnosed in young people in Australasia and the prevalence is unknown. We also don't know if there is a clear link between manic symptoms in childhood with adult bipolar disorder.

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- On the one hand, the estimated prevalence of bipolar disorder among adults in New Zealand is 1.5 %, with a mean age of onset of 18 years.⁽¹⁾
- On the other hand, Australasian adolescent onset bipolar disorder has been reported in several studies. Two different studies, one in Auckland (Werry et al.²) showed 9 years-old as the lowest age of onset in 23 patients managed over 20 years of period.
- The second one, conducted in Sydney (Bashir et al.³) confirmed, as the previous one, that 50 % of the sample with bipolar disorder was initially diagnosed with schizophrenia.

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- In 2003, a group from Newcastle (Australia₁) illustrated that 21 % of patients admitted to their Unit received diagnosis of bipolar disorder; while 10 % were thought to have sub clinical or prodromal bipolar disorder. ⁽¹⁾
- This last cohort was characterized by being predominantly female, with affective instability, irritability, self-harming and assaultive behaviours in the background of domestic violence and sometimes homeless. Whether these symptoms could be explained by bipolarity or by other mechanisms such as dissociation is debatable again.

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- A cross sectional study replicated in Australia and US (Hazell et al.) by using the Child Behaviour Checklist (CBCL) found mania symptoms in one of five children diagnosed with ADHD/hyperactivity disorder. Childhood history of mania was predictive of poorer functioning at follow up after six years, but did not predict psychiatric diagnosis. Most cases of pre pubertal paediatric bipolar disorder were first diagnosed with ADHD or depression.⁽¹⁾

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- Birmaher, B (Pittsburgh, PA) examined in his COBY study (Course and Outcome of Bipolar Youth) every month for 10 years: 58 % bipolar I children, 7 % bipolar II, and 35 % bipolar NOS. He found that BPNOS (86%) met severity criteria for BP I or II but fell short of the duration required. 66% recovered in 2 years and 48 % had at least one recurrence. Poorer outcome at 2 years included early-onset, psychosis, diagnosed by BPNOS, having mixed episodes, lower social economic status, co morbid anxiety and ADHD. Children with BPI are more likely to have mixed episodes, rapid cycling, fewer periods of wellness, more fluctuations in polarity.⁽⁵⁾

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- Liebenluft et al., (Bethesda, US) have indicated that “irritability” is a target symptom in childhood bipolarity. According to DSM IV TR, irritability is a core criteria in oppositional defiant disorder (ODD), major depressive disorder (MDD) and mania. In relation to this classification, irritability qualifies only in childhood as unique criteria for MDD. Besides, it is a major cause of morbidity and distress among children with pervasive developmental disorder (PDD), anxiety disorders, and attention deficit hyperactive disorder (ADHD) (8,9)

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- **Irritability** can be defined as an emotional state characterized by having a low threshold for experiencing anger in response to negative emotional events.
 - Anger is a dysphoric state associated with aggressive impulses. There is a continuum from subjective experience to behaviour response that includes verbal and/or physical aggression.
 - Children with depression could manifest irritability with labile sadness, sudden onset of tearfulness or social withdrawal.
 - Children with mania, on the other hand, express irritability with labile sadness and labile euphoria(suddenly elated or silly state)
 - In paediatric mania irritability is **episodic** not chronic.
- Episodic irritability** in early adolescence was associated with BPD and anxiety disorders in late adolescence with BPD in adulthood.
- Chronic irritability** in early adolescence was associated with ODD and ADHD in late adolescence and MDD in adulthood.(8,9)

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- DSM IV TR ⁽¹⁰⁾ reveals that the “A” criteria for a manic episode requires “an abnormally, persistently elevated, expansive or irritable mood” lasting at least one week for mania and four days for hypo mania or (any duration if hospitalization is necessary). Whether irritability alone should diagnose juvenile mania or whether episodic or chronic irritability should be sufficed, is again unclear.
- Liebenluft, E. et al. pointed out differences between non episodic irritability and childhood bipolar disorder. They defined two possible phenotypes of BP:
 - Narrow phenotype based on DSM IV classification
 - Broad phenotype (Severe Mood Dysregulation).^(8,9)

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SEVERE MOOD DYSREGULATION- BROAD PHENOTYPE

Liebenluft inclusion criteria:

- Aged 7 -17, with the onset of symptoms before age 12

a) Abnormal mood (specifically, anger or sadness) present at least half of the day most days, and of sufficient severity to be noticeable by people in the child's environment (e.g. parents, teachers, peers)

b) Hyper arousal, as defined by at least three of the following: insomnia, agitation, distractibility, racing thoughts or flight of ideas, pressured speech, intrusiveness.

c) Compared to his/her peers, the child exhibits markedly increased reactivity to negative emotional stimuli that is manifest verbally or behaviourally. For example, the child responds to frustration with extended temper tantrums (inappropriate for age and/or aggression toward people or property. Such events occur, on average, at least three times a week.

- The symptoms noted in a), b) and c) above are currently present and have been present for at least 12 months, without any symptom-free periods exceeding two months.
- The symptoms are severe in at least one setting (e.g. violent outbursts, assaultiveness at home, school, or with peers) In addition; there are at least mild symptoms (distractibility, intrusiveness) in a second setting.

Exclusion criteria in the Broad phenotype.

- The individual exhibits any of these cardinal bipolar symptoms by DSM IV.
- The patient's illness meets criteria for schizophrenia, schizophreniform disorder, schizoaffective illness, PDD, or PTSD.
- Patient's symptoms would meet criteria for substance use disorder in past 3 months.
- IQ < 80
- The symptoms are due to the direct physiological effects of a drug of abuse, or to a general medical or neurological condition. (8,9)

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Objectives

The aim of this paper is to discuss diagnostic indicators for paediatric bipolar disorder based on our clinical practice. It is hoped to help researchers and clinicians to detect this disorder earlier in age and to establish an adequate treatment.

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Methods.

This is an initial investigation and study that will guide us to build knowledge for further researches in this area. We have diverse limitations in this paper, because it is a retrospective study and 4 year -follow up of our patients. They were diagnosed by an interdisciplinary team using DSM IV and Liebenluft criteria.

We analysed a sample of N: 287 subjects between 7 to 20 years of age, who were admitted to Mackay Base Hospital from 2002 to 2006. Mackay is a regional area in Central Queensland (Australia) with 150.000 Inhabitants and 20% Indigenous and TSI population.

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Methods.

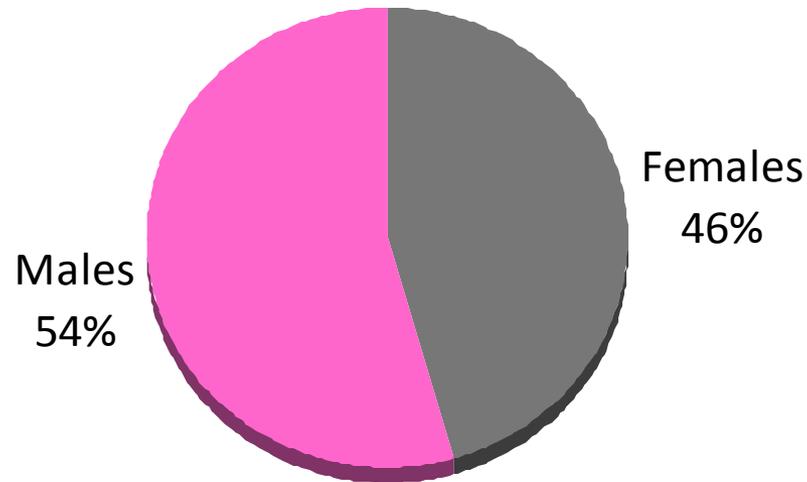
Mackay is a regional area in Central Queensland (Australia) with 150,000 inhabitants and 20% Indigenous and TSI population.



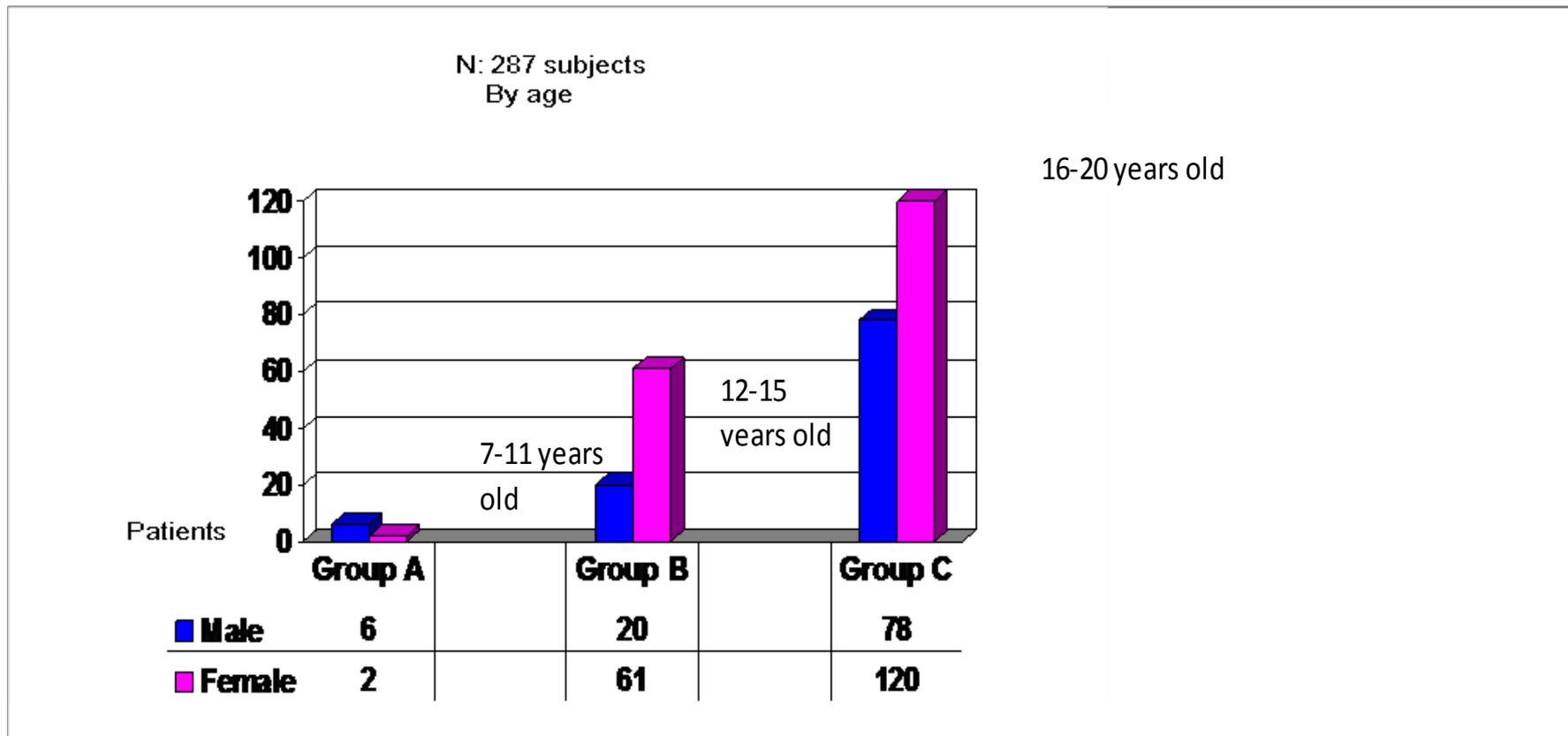
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Results.

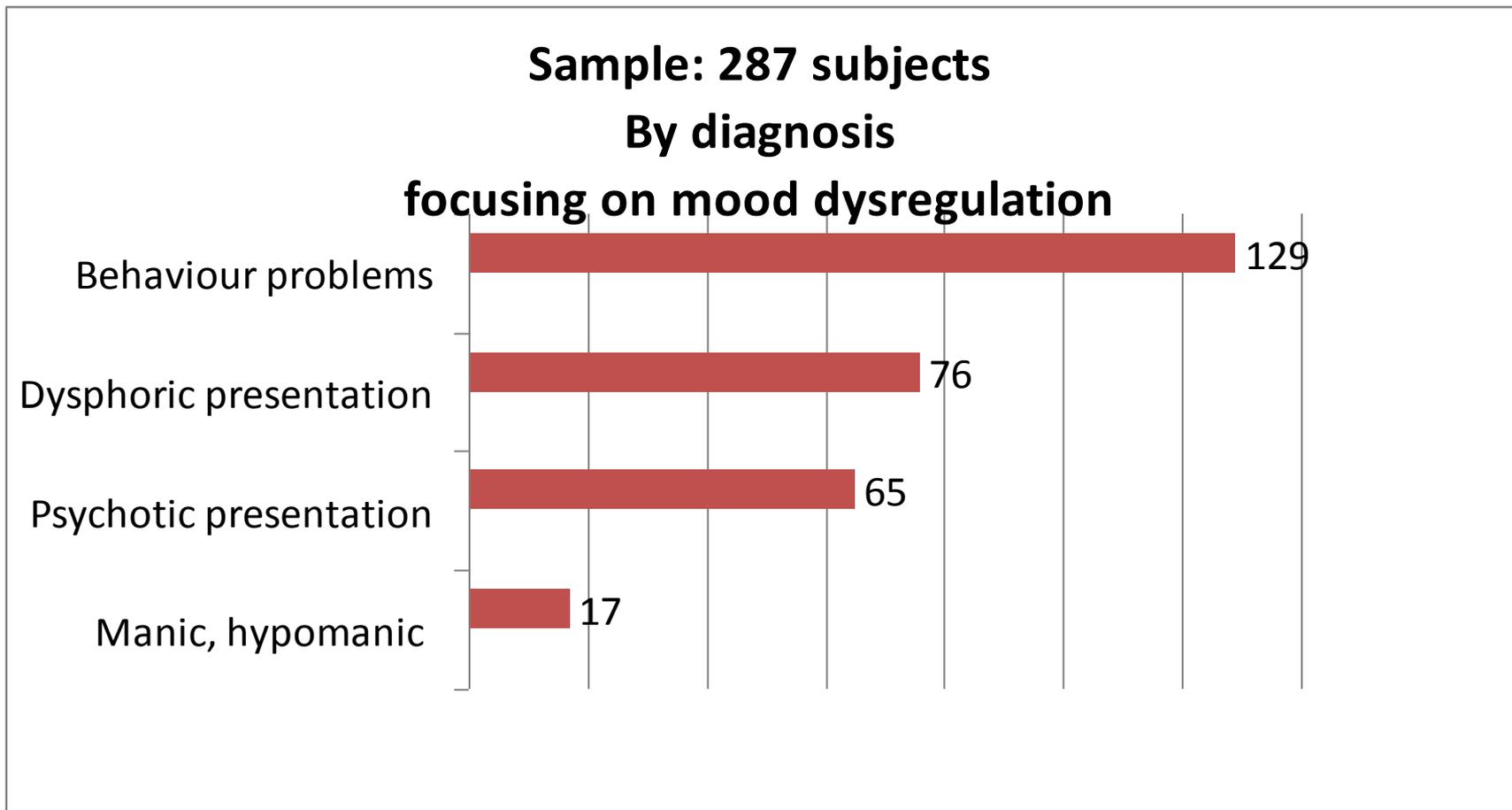
Sample: 287 subjects
2002-2006
Admitted in MBH
By gender



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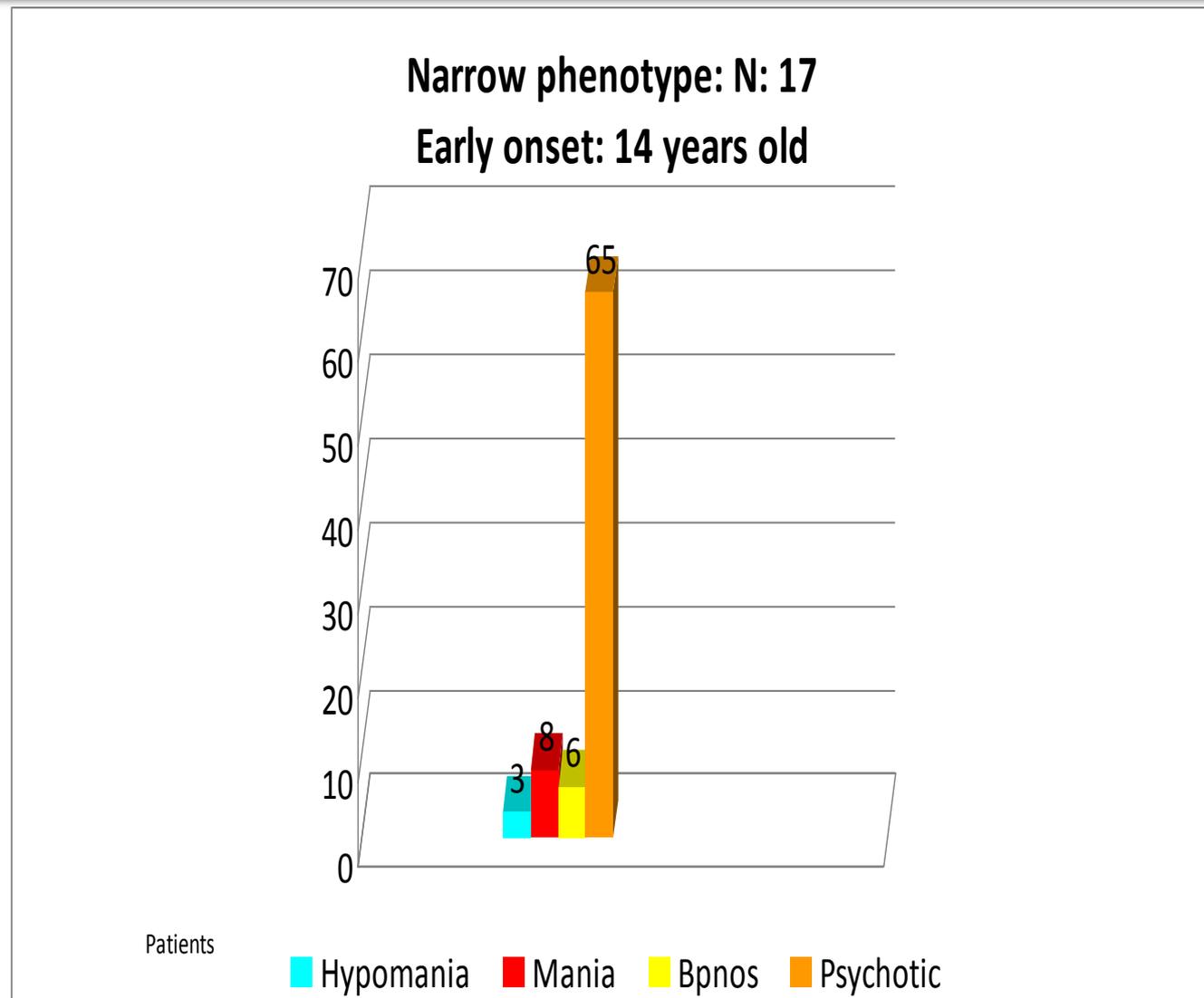


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History of mania or hypo mania, BPNOS and schizophreniform disorders that met full DSM IV criteria.

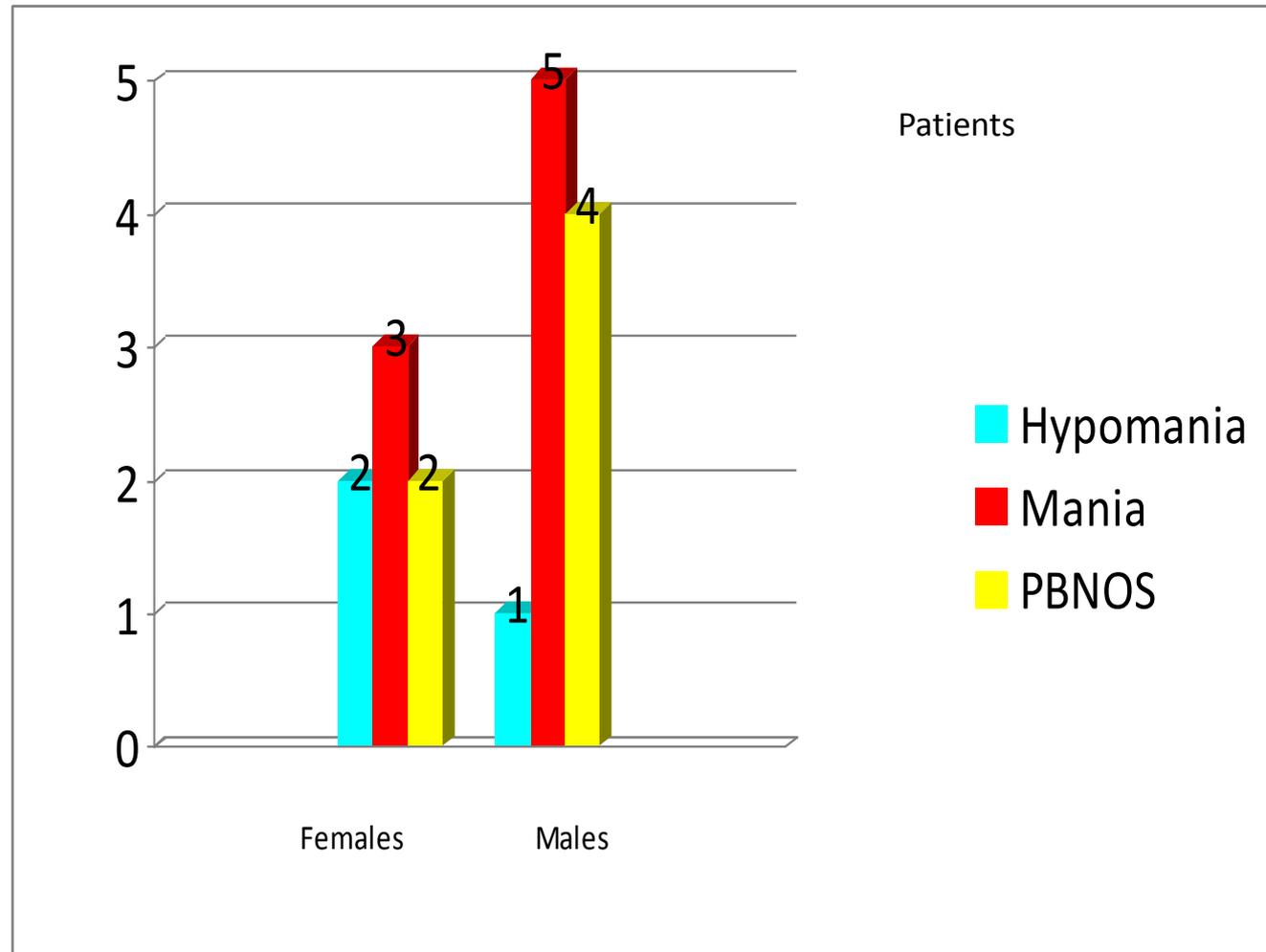


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NARROW PHENOTYPE

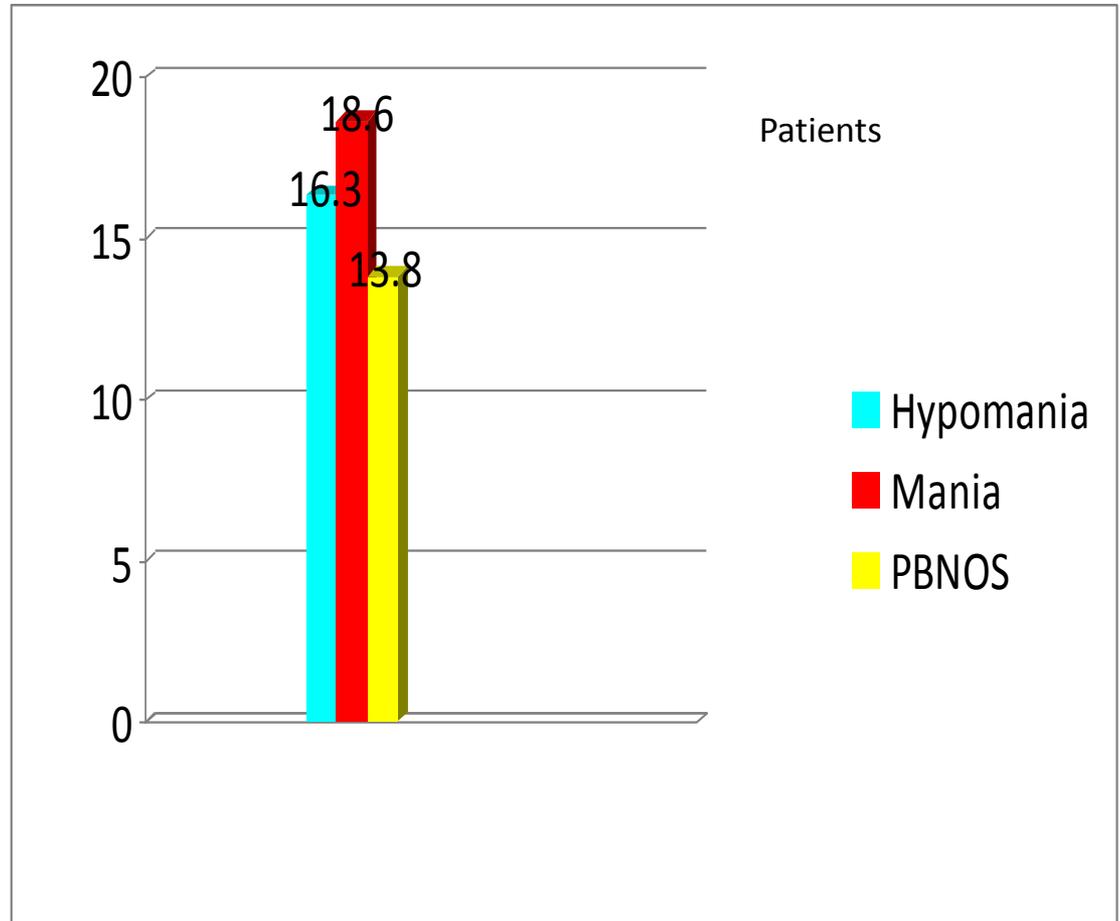
N: 17

Prevalence is slightly
higher in males for
Mania and
BP NOS.



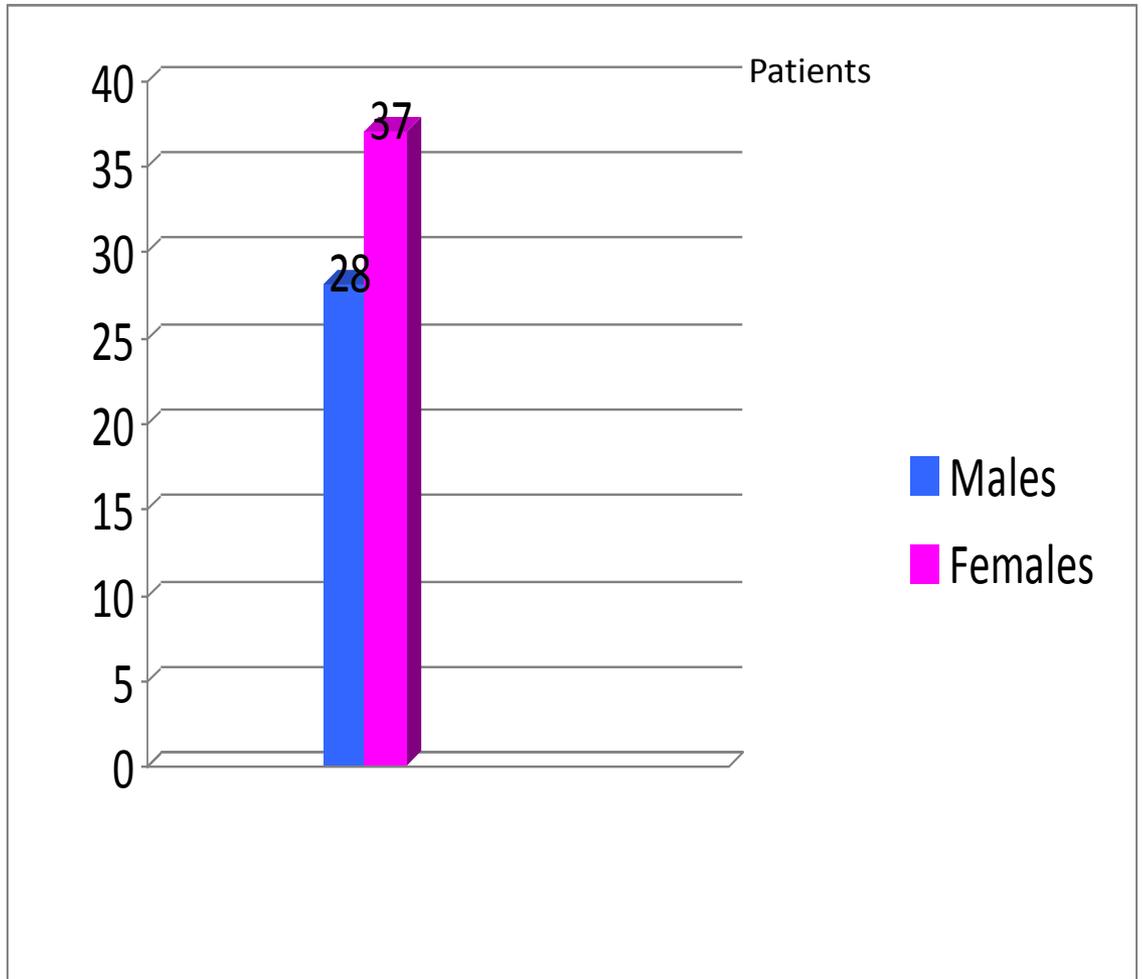
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Mean age for mania is older than for hypomania and BPNOS.



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Schizophreniform disorders were dramatically higher in females. The mean age of onset was 18.6 years old with an early onset of 14 years old.



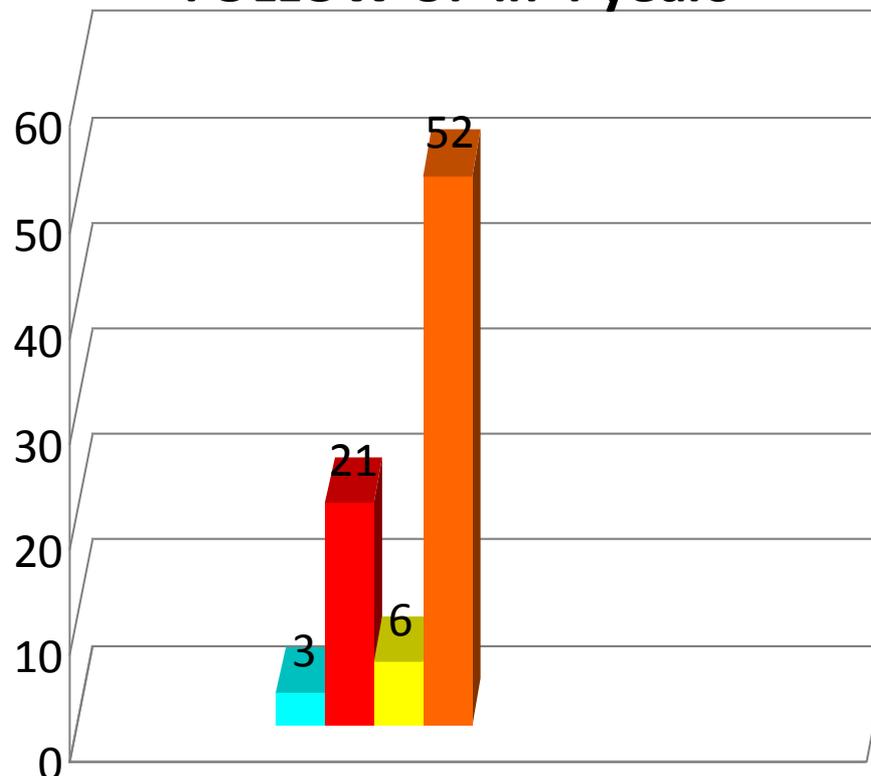
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Mc Gorry et al.(Melbourne)(12) pointed out that early phases of bipolar disorders are difficult to diagnose and have specific treatment issues. The initial polarity of the illness is more commonly misdiagnosed. There is an important delay before starting with appropriate therapy until mania is evident and required for the diagnose.

In our sample after 4 years of follow up, 20 % (13 cases) with first psychotic symptomatology, became bipolar with manic presentations. We observed in their retrospective histories that 2 of the cases had ADHD, 10 cases exhibited disruptive behaviours, and 80 % of the cases had history of poly substance abuse before the age of the first admission in the Hospital.

30% had family history of mood disorders noted in the charts.

Narrow phenotype: N: 30 FOLLOW UP in 4 years

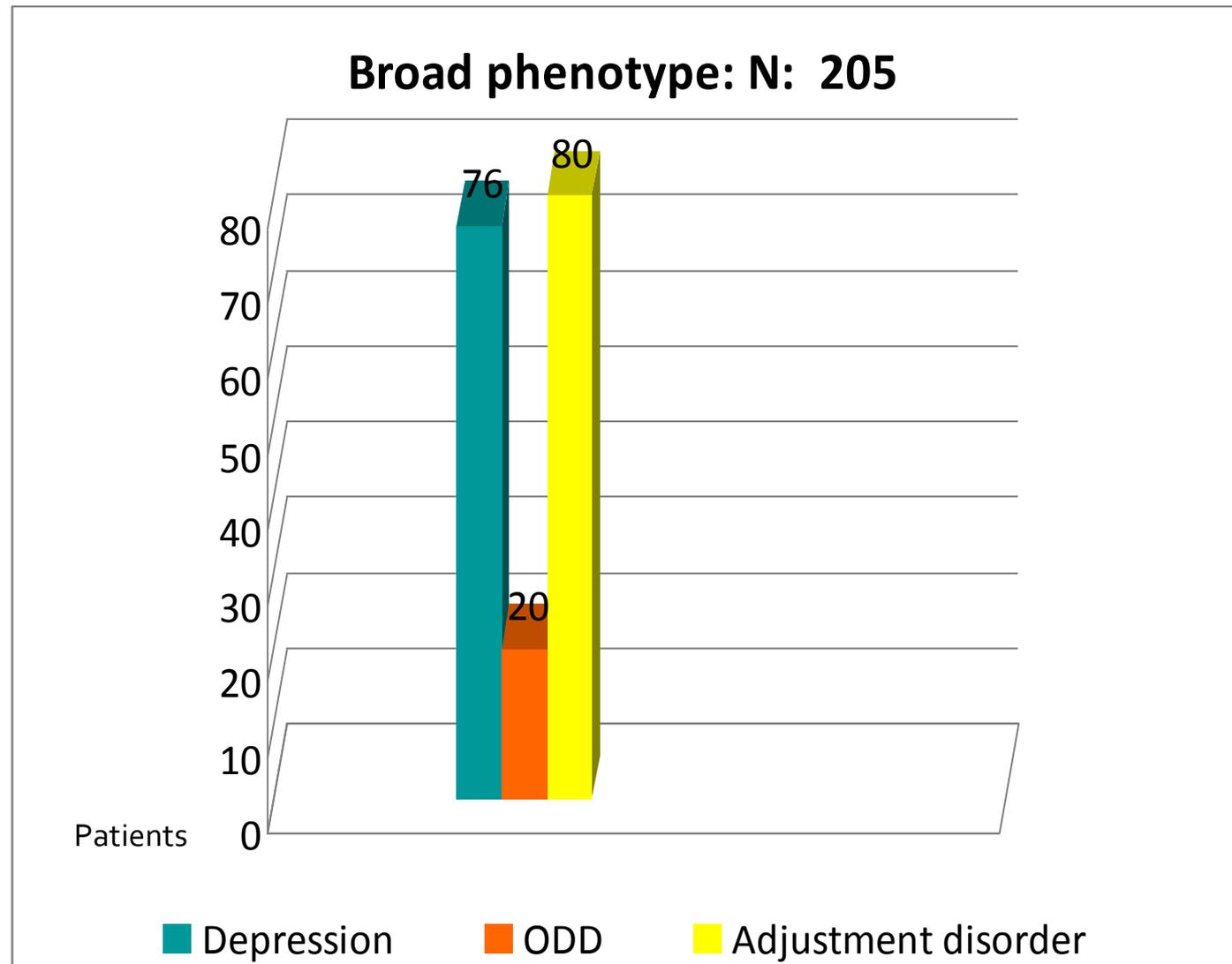


■ Hypomania ■ Mania ■ Bpnos ■ Psychotic

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Different presentations with Adjustment Disorders and Depressive Disorders with dysphoric mood.

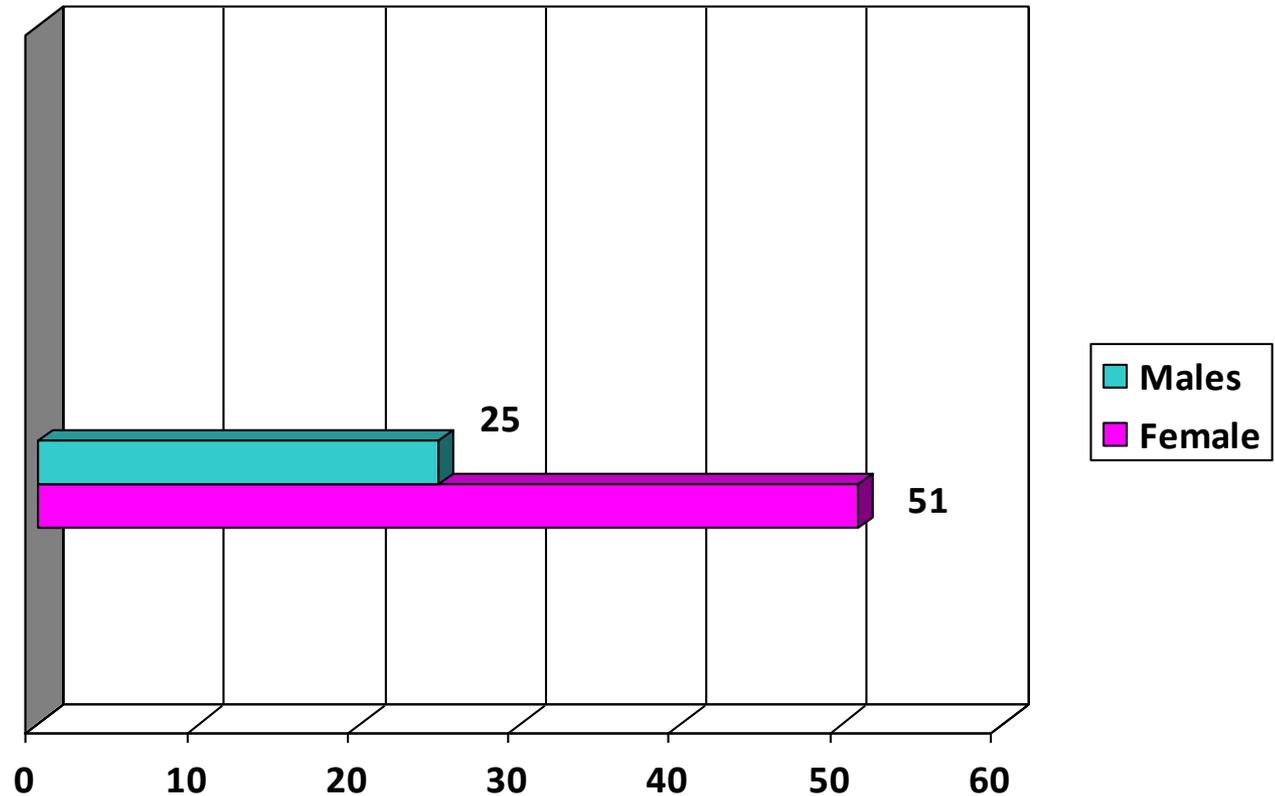
20 cases were admitted due to ODD.



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MOOD DISORDERS

76 mixed patients with presentations of depression with dysphoric mood and episodic irritability in the background of chronic psychosocial stressors. Mean age 15 years old and females doubled males in this group.

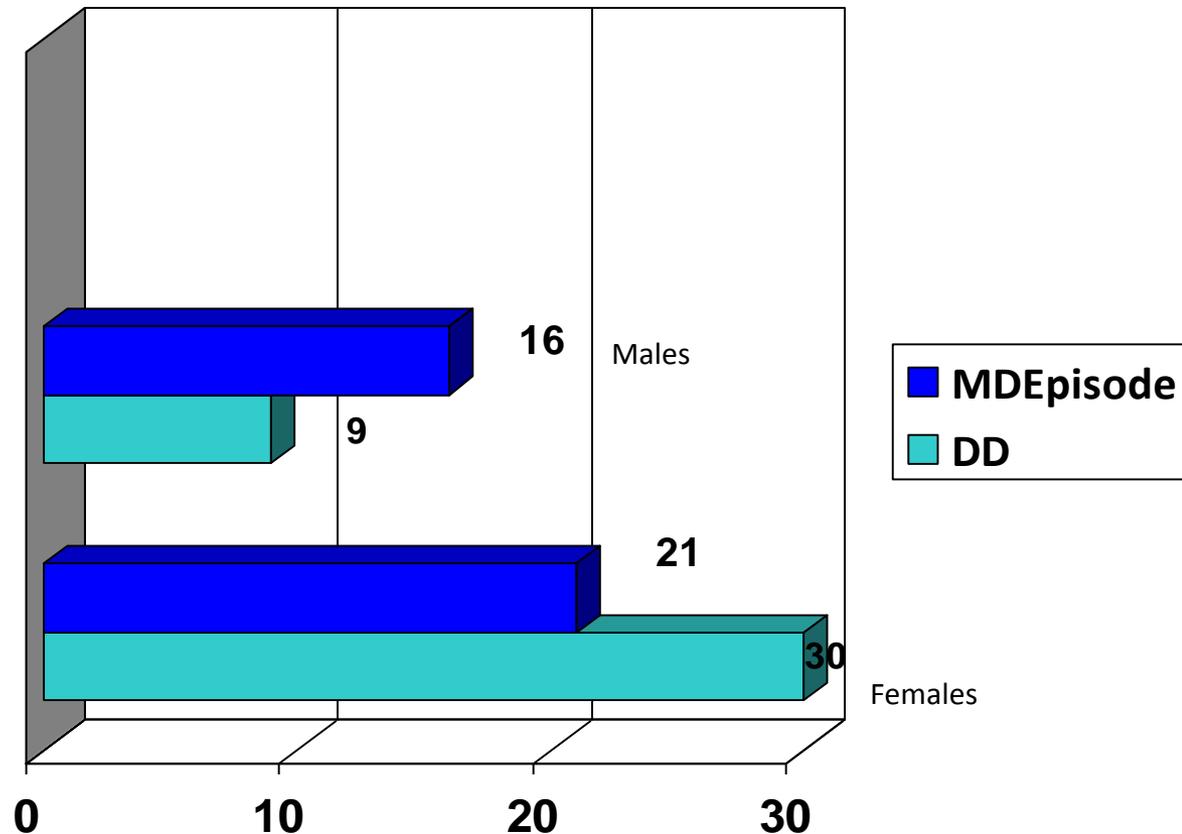


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DYSPHORIC MOOD

Dysthymia was important in this sample.
Double depression versus first MDE.

No one of these group switched to mania/hypomania in 4 years of follow up. More than 60 % of the cases had family history of mood disorders.

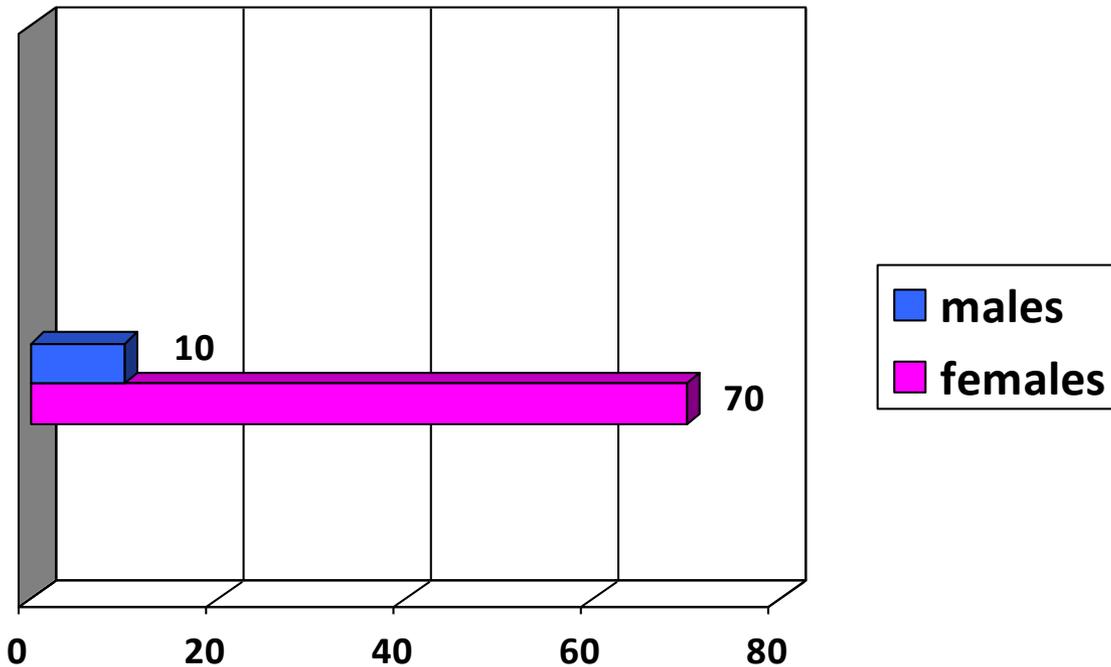


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ADJUSTMENT DISORDERS

80 cases of adjustment disorders with history of self harming behaviours and mood instability and were thought as Cluster B axis II.
Mean age: 16.3 years of age.

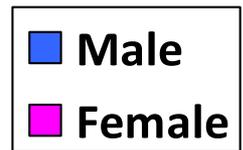
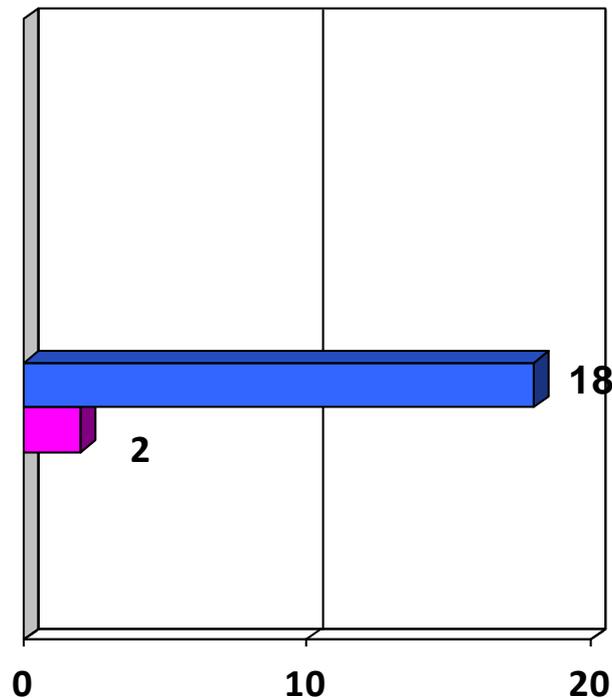
This is another controversial group. The instability of the mood was evident. In 4 years, we did not see evidence of a switch of mania or Hypomania. They maintained their mood instability and episodic irritability.



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18 male patients, mean age 8 years old, exhibited chronic irritability, hyper arousal, and hyper reactivity to negative emotional stimuli without grandiosity or elation. 40% had depression like irritability. In 90% of the cases we observed severe attachment disorders. Strong family history of mood disorders and poly substance abuse. 3 cases has different admissions due to self harming behaviours, and aggressive presentations. Mood instability and irritability were evident. Poor response to medication, case management and family therapy.

BROAD PHENOTYPE: ODD



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DISCUSSION

- Irritability has different faces in our clinical experience; with an spectrum from normal irritability to severe mood dysregulation. Children with normal development exhibit an increasing ability to control their impulses facing adversity.
- We would need to find an adequate instrument to score and compare “irritability” in these children.
- Davidson’s affective chronometry (8) suggested differences in emotional reactivity in bipolar children comparing with normal ones. Bipolar children differ in the threshold that such stimuli must exceed to elicit a response, as well as in the duration and amplitude of their response.

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DISCUSSION

- fMRI work indicates that high levels of reactive aggression have reduced frontal lobe activity. Conversely, violent individuals with goal directed instrumental aggression show appropriate frontal activity. fMRI shows in bipolar children difficulties to recognize “angry faces” comparing with normal children. Bipolar children misidentify anger in peers’ faces, specifically misidentifying other expressions (happy, fearful, or sad).
- Psychological studies based on frontal lobe dysfunction, go no go, plus concepts of executive functioning (inhibition, working memory, organization time, emotional self-control, self motivation, and planning) could be promising to distinguish types of BP in children.

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DISCUSSION

- Children with broad or narrow phenotype are severely impaired.
- Different approaches are possible to offer if we could diagnose Bipolar disorders in early age.
- Narrow phenotype was possible to detect in late adolescence or early adulthood. What happened with them in childhood?
- Should the same criteria be used to diagnose BP in adults and children?
- Is the same evidence to justify a BP diagnosis for children who do not meet adult criteria?
- Should SMD children be diagnosed with BP or is this a new category?

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Conclusion

Results show irritability as an important feature in this debate. Perhaps future researches in children with severe mood dysregulation will guide us in the cross road of this controversial topic.

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