

# EVALUATION OF THE BROAD PHENOTYPE OF BIPOLAR DISORDER INTO YOUNG ADULTHOOD



Robert R. Althoff, M.D., Ph.D.<sup>1</sup>, Dorret I. Boomsma, Ph.D.<sup>2</sup>,

and James J. Hudziak, M.D.<sup>1,2</sup>

University of Vermont College of Medicine<sup>1</sup> and The Free University, Amsterdam, The Netherlands<sup>2</sup>

## INTRODUCTION

• There has been considerable debate about the broad phenotype of bipolar disorder (BD-BP), particularly in Juvenile Bipolar Disorder (JBD)

• The Child Behavior Checklist (CBCL-JBD) has been used to screen for or to provide additional information to the clinician for BD-BP

Regardless of their name, these children are common in the clinic and are significantly
more impaired than their counterparts without this combination

• We have also demonstrated clear environmental components to the expression of the phenotype at younger ages, with reduction into early adolescence

• 17-22% of children ages 7-12 with this CBCL-JBD express suicidality by parental report, likely an underestimate of the true amount of suicidality

• We have examined this phenotype only in the child population, whereas there are significant increases in the prevalence of true mania as adolescence proceeds

· Little is known about the progression of the BD-BP into early adulthood

#### SAMPLE

2856 twin pairs aged 18-24 from the Adult Netherlands Twin Registry were examined, including 482 MZ male, 430 DZ male, 660 MZ female, 490 DZ female, and 794 DZ opposite sex pairs. The twins were recruited from local city councils. All participation was voluntary and approved by the IRB of the Vrije University, Amsterdam

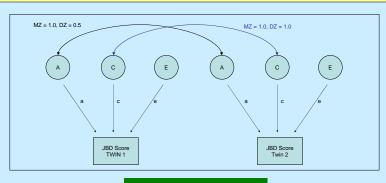
#### MEASURES

Participants in the study were asked to complete the Young Adult Self Report form of the CBCL family of instruments. This consists of 118 items which are similar to the Youth Self Report form and the summary scales have been constructed similarly. We examined here the Attention Problems (AP), Aggressive (AGG) and Anxious/Depressed (A/D) scales. Additionally, we examined items #18 ("I deliberately harms myself or attempt suicide") and #91 ("I talk about killing myself") as measures of suicidal thoughts and behavior.

## DATA ANALYSIS

Data from the AP, A/D, and AGG scales were combined into a summed score. This score was square-root transformed because of its skewed distribution. Those data were subjected to Structural Equation Modeling (SEM) using the program Mx [7]. The basic model is shown below. Models were compared by adding or removing components and comparing changes in the -2ll between models, which is distributed as a chi-square. When comparing models, therefore, a p value > 0.05 means that the models are the same, while a p value < 0.05 means that the models are different. The best fitting model was chosen and estimates of Additive Genetic (A), Common Environmental (C) and Unique Environmental (E, which also includes error) were determined.

Disclosures : This research was supported by grants NIMH MH58799, NWO 904-57-94, NWO 575-25-006 and the Centre for Neurogenomics and Cognition Research (CNCR).



#### RESULTS

About 0.8% of the sample met T score criteria for the phenotype, regardless of gender
37.5% of the men and 40% of the women with the BD-BP endorsed suicidal ideation
Model fits revealed an AE model for males and females, separately (Tables 1 and 2)

#### Table 1. Model fits

$\begin{tabular}{ c c c c c c c c c c c c c c c c c c c$								Compared
2         ACE         14613.36         18         13.368         12         0.34         1           3         ACEi         14613.18         19         0.181         1         0.67         2	Model #	del # Model	-211	# param	χ2	∆df	р	to model
3 ACEi 14613.18 19 0.181 1 0.67 2	1	1 Full Sat	14599.99	30				
	2	2 ACE	14613.36	18	13.368	12	0.34	1
4 AE 14613.8 16 0.438 2 0.80 2	3	3 ACEi	14613.18	19	0.181	1	0.67	2
	4	4 <i>AE</i>	14613.8	16	0.438	2	0.80	2
5 AEi 14613.55 17 0.243 1 0.62 4	5	5 AEi	14613.55	17	0.243	1	0.62	4
6 CE 14675.49 16 62.129 2 0 2	6	6 CE	14675.49	16	62.129	2	0	2
7 AE no sex 14628.1 14 14.307 2 0.00 4	7	7 AE no sex	14628.1	14	14.307	2	0.00	4

#### Table 2. Model estimates from best fitting model

	Female	Male
Additive Genetic (A)	0.60 (0.55 - 0.64)	0.47 (0.40 - 0.54)
Unique Environmental (E)	0.40 (0.36 - 0.45)	0.53 (0.46 - 0.60)

## DISCUSSION

•Young Adult Self-Report identifies a profile similar to the CBCL-JBD phenotype

•Shared environmental effects, present in younger twins, diminish by age 12 and are absent in adulthood

•The characteristics of the disorder, including the percentage of the sample presenting with the disorder, the magnitude of heritability, and the association with increased suicidal thinking make it probable that there is continuity of the disorder from childhood to adulthood

•More work needs to be done to characterize how this constellation of symptoms is related to other diagnoses (such as personality disorders, depressive disorders, mania)