

QU'ADVIENT-IL DES ADOLESCENTS BIPOLAIRES À L'ÂGE ADULTE ?

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PLAN

- **Introduction**
- **Les principales études de la littérature**
- **BD-I sévères chez l'adolescent: index épisode**
- **BD-I sévères chez l'adolescent : devenir**
- **Facteurs associés d'une transition SCZ**
- **Conclusion**



MEDECINE/SCIENCES 2009 ; 25 : 534-6

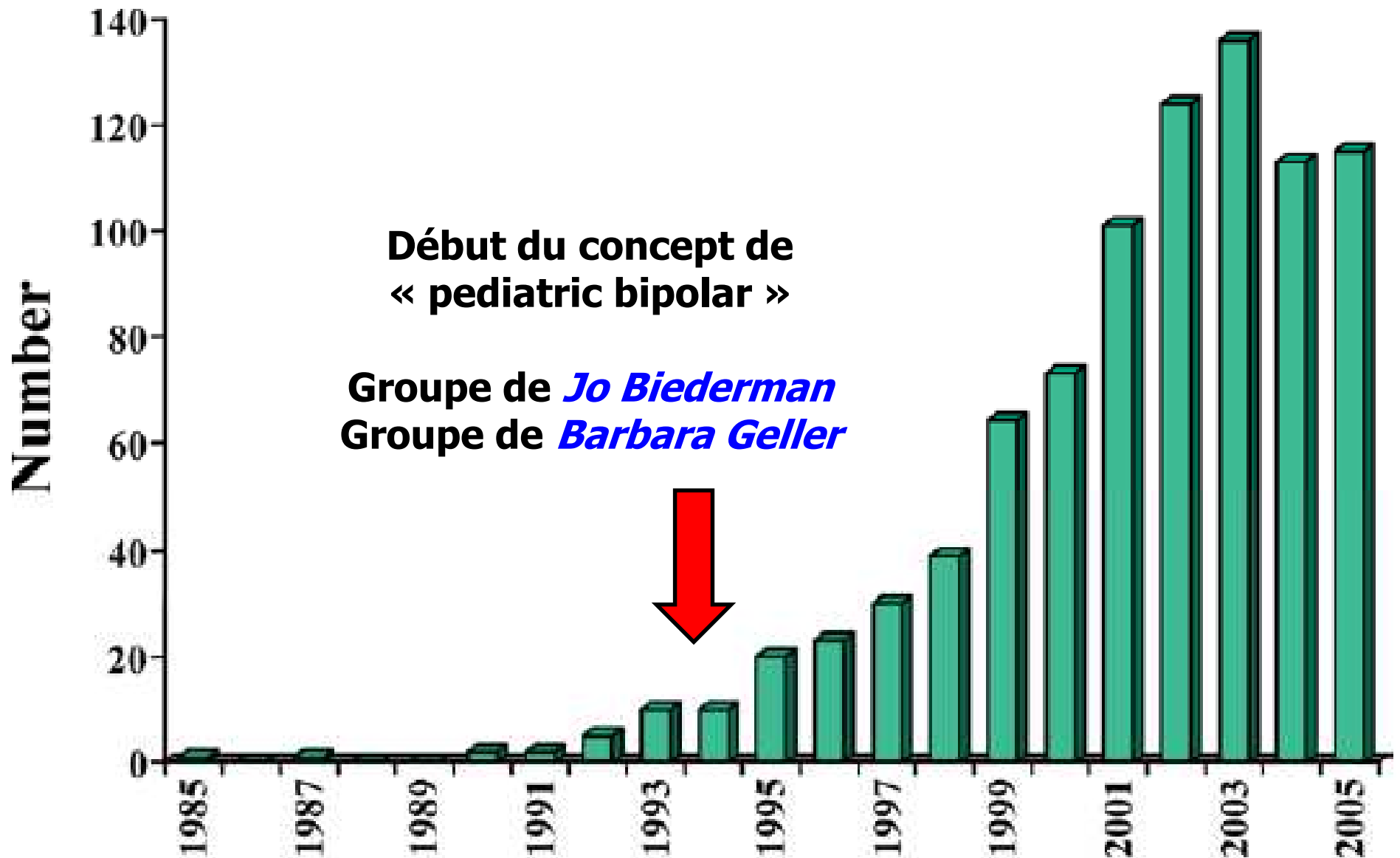
La pédopsychiatrie américaine au ban des accusés

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Figure 1. Articles Elicited by Medline Using the Mesh Term "Mood Stabilizer"

Healy, PlosMed, 2006

Problèmes diagnostiques et controverses

<i>Symptômes maniaques de l'enfant</i>	<i>Episodes maniaques de l'adolescent</i>
Chronique et continu	Episodique
Comorbidité élevée au TDAH	ATCDs de TDAH marginaux
Symptômes psychotiques exceptionnels	30 à 60% de symptômes psychotiques
ATCDs familiaux très variés	ATCDs familiaux de bipolarité
Facteurs environnementaux au premier plan et troubles des apprentissages fréquents	Fonctionnement prémorbide souvent de bonne qualité



Geller and Luby, 1997

Charfi & Cohen, 2005

Carlson, 2005

The Clinical Phenotypes of Juvenile Bipolar Disorder Toward a Validation of the Episodic-Chronic- Distinction

	Episodic		Chronic		<i>F/χ²</i>	<i>p</i>
	Elated <i>n</i> = 50	Irritable <i>n</i> = 27	Elated <i>n</i> = 25	Irritable <i>n</i> = 34		
Age, Mean (SD)	14.7 (2.7)	14.4 (2.3)	12.4 (3.1)	11.9 (2.6)	10.1	.000 ^{ab}
Age Onset, Mean (SD)	12.1 (2.7)	10.9 (3.1)	7.8 (3.2)	8.6 (2.5)	17.6	.000 ^{ab}
Gender, Males (<i>n</i> , %)	30 (60.0)	19 (70.4)	14 (56.)	18 (52.9)	2.1	.765
C-GAS Baseline, Mean (SD)	43.4 (9.3)	41.8 (7.6)	40.5 (6.5)	41.3 (5.5)	1.0	.406
CGI-S Baseline, Mean (SD)	5.2 (1.0)	5.0 (1.0)	5.5 (.7)	5.0 (.6)	2.0	.114
CGI-I (6-Month), Mean (SD)	2.12 (.7)	2.18 (.6)	2.56 (.8)	2.48 (.7)	3.4	.019 ^a
Lifetime Comorbidity, <i>n</i> , (%)						
Social Phobia	16 (32.0)	6 (22.2)	6 (24.0)	6 (17.6)	2.4	.671
Panic Disorder	16 (32.0)	4 (14.8)	5 (20.0)	7 (20.6)	3.5	.439
Separation Anxiety	11 (22.0)	5 (14.8)	7 (28.0)	4 (11.8)	2.6	.619
Obsessive-Compulsive Disorder	24 (48.0)	15 (55.5)	10 (40.0)	11 (32.3)	3.8	.379
Generalized Anxiety Disorder	14 (28.0)	10 (37.0)	10 (40.0)	11 (32.4)	1.5	.917
ADHD	7 (14.0)	6 (22.2)	10 (40.0)	13 (38.2)	9.0	.037 ^a
Conduct Disorder	4 (8.0)	3 (11.1)	4 (16.0)	10 (29.4)	9.4	.072
Oppositional-Defiant Disorder	8 (16.0)	6 (22.2)	11 (44.0)	9 (26.5)	7.1	.089
Total Number						
Anxiety Disorders	1.7 (1.2)	1.4 (1.3)	1.3 (1.3)	1.2 (1.2)	1.1	.061
Externalizing Disorders	.4 (.7)	.6 (.6)	1.0 (.8)	1.0 (.8)	6.3	.000 ^{ac}

C-GAS, Children's Global Assessment Scale; CGI-S, Clinical Global Impression-Severity; CGI-I, Clinical Global Impression-Improvement; ADHD, attention-deficit/hyperactivity disorder.

^aStatistically significant ($p < .05$).

^bPairwise comparison (Tukey), significant difference between Episodic Elated (both Elated and Irritable) and Chronic (both Elated and Irritable) and between Episodic Irritable and Chronic Irritable.

^cPairwise comparison (Tukey), significant difference between Episodic (both Elated and Irritable) and Chronic (both Elated and Irritable).

^dPairwise comparison (Tukey), significant difference between Episodic Elated and Chronic (both Elated and Irritable).

Masi et al, 2006, Biol Psychiatry

Adult Outcomes of Youth Irritability: A 20-Year Prospective Community-Based Study

Argyris Stringaris, M.D.,
M.R.C.Psych.

Patricia Cohen, Ph.D.

Daniel S. Pine, M.D.

Ellen Leibenluft, M.D.

Objective: Irritability is a widely occurring DSM-IV symptom in youths. However, little is known about the relationship between irritability in early life and its outcomes in mid-adulthood. This study examines the extent to which youth irritability is related to adult psychiatric outcomes by testing the hypothesis that it predicts depressive and generalized anxiety disorders.

Method: The authors conducted a longitudinal community-based study of 631 participants whose parents were interviewed when participants were in early adolescence (mean age=13.8 years [SD=2.6]) and who were themselves interviewed 20 years later (mean age=33.2 years [SD=2.9]). Parent-reported irritability in adolescence was used to predict self-reported psychopathology, assessed by standardized diagnostic interview at 20-year follow-up.

Results: Cross-sectionally, irritability in adolescence was widely associated with other psychiatric disorders. After adjustment for baseline emotional and behavioral disorders, irritability in adolescence predicted major depressive disorder (odds ratio=1.33, 95% confidence interval [CI]=1.00–1.78), generalized anxiety disorder (odds ratio=1.72, 95% CI=1.04–2.87), and dysthymia (odds ratio=1.81, 95% CI=1.06–3.12) at 20-year follow-up. Youth irritability did not predict bipolar disorder or axis II disorders at follow-up.

Conclusions: Youth irritability as reported by parents is a specific predictor of self-reported depressive and anxiety disorders 20 years later. The role of irritability in developmental psychiatry, and in the pathophysiology of mood and anxiety disorders specifically, should receive further study.

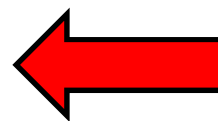
TABLE 1. Association of Parent-Rated Irritability With Diagnoses in Early Adolescence^a

Diagnosis	Odds Ratio	95% CI
Major depressive disorder	2.134***	1.54–2.96
Overanxious disorder	1.443***	1.19–1.75
Conduct disorder	1.947***	1.57–2.42
Oppositional defiant disorder	3.661***	2.85–4.71
Simple phobia	1.335**	1.08–1.65
Social phobia	1.465**	1.16–1.85
Attention deficit disorder	1.864***	1.51–2.30
Bipolar disorder	1.781***	1.38–2.30

^a Logistic regression models adjusted for age, sex, and socioeconomic status presented for each diagnosis with parent-reported irritability as the dependent variable. N=756.

p<0.01; *p<0.001.

**Diagnosics
associés
vers 12 ans**



**Diagnosics
associés
20 ans plus tard**

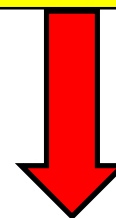


TABLE 2. Irritability in Early Adolescence as Predictor of Disorders at 20-Year Follow-Up^a

Disorder in Adulthood	Adjustment for Disorders in Early Adolescence					
	Not Adjusted		Emotional Disorders		Emotional and Behavioral Disorders	
	Odds Ratio	95% CI	Odds Ratio	95% CI	Odds Ratio	95% CI
Major depressive disorder	1.48***	1.16–1.89	1.41*	1.08–1.84	1.33*	1.00–1.78
Generalized anxiety disorder	2.11***	1.37–3.24	1.93**	1.19–3.13	1.72*	1.04–2.87
Dysthymia	2.07***	1.34–3.20	2.07**	1.32–3.26	1.81**	1.06–3.12
Bipolar disorder	1.31	0.77–2.24	1.18	0.57–2.44	1.02	0.39–2.69
Axis II disorders	1.03	0.81–1.31	0.97	0.81–1.26	0.85	0.63–1.15

^a All logistic regression models report unit-based increases in irritability associated with increases in the odds of disorder in adulthood, adjusted for age, sex, and family socioeconomic status. Imputed N=776.

*p<0.05; **p<0.01; ***p<0.001.



Parental Diagnoses in Youth With Narrow Phenotype Bipolar Disorder or Severe Mood Dysregulation

Objective: Controversy exists regarding whether nonepisodic irritability and hyperarousal (severe mood dysregulation) is a phenotype of pediatric bipolar disorder. The authors compared axis I diagnoses in parents of children with narrow phenotype bipolar disorder and parents of youth with severe mood dysregulation.

Method: Parents of youth with narrow phenotype bipolar disorder (proband N=33, parent N=42) and youth with severe mood dysregulation (proband N=30, parent N=37) were interviewed by clinicians who were blind to the child's diagnostic status using the Diagnostic Interview for Genetic Studies.

Results: Compared to parents of youth with severe mood dysregulation, parents of youth with narrow phenotype bipolar disorder were significantly more likely to be diagnosed with bipolar disorder. There were no other diagnostic differences between the two groups.

Conclusions: These data suggest that narrow phenotype bipolar disorder may be distinct from severe mood dysregulation in terms of familial aggregation. Additionally, the familiarity of narrow phenotype bipolar disorder and adult DSM-IV bipolar disorder is high.

Adolescence marks the beginning of the high-risk period for major mood episodes related to family history of bipolar disorder

Early course of bipolar disorder in high-risk offspring: prospective study

Anne Duffy, Martin Alda, Tomas Hajek and Paul Grof

Summary

We studied the course of major mood disorders in the offspring of parents with well-characterised bipolar disorder prospectively for up to 15 years. All consenting offspring were assessed annually or anytime symptomatic. The participants began to develop major mood episodes in adolescence and not before. The index major mood episode was almost always depressive, as were the first few recurrences. Onsets and recurrences continued

throughout the observation period into adulthood. We did not find evidence of pre-pubertal mania. In summary, adolescence marks the beginning of the high-risk period for major mood episodes related to bipolar disorder.

Declaration of interest

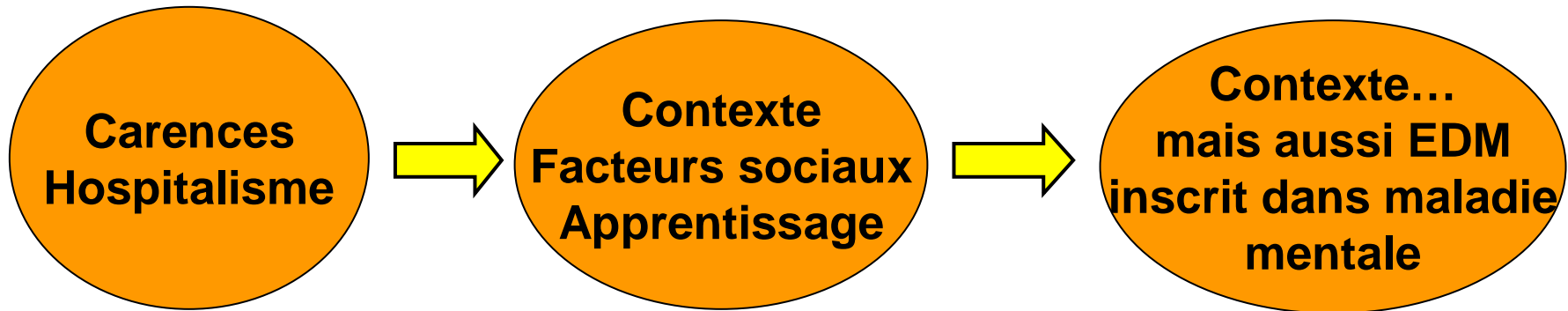
None.

Duffy et al, Br J Psy, 2009

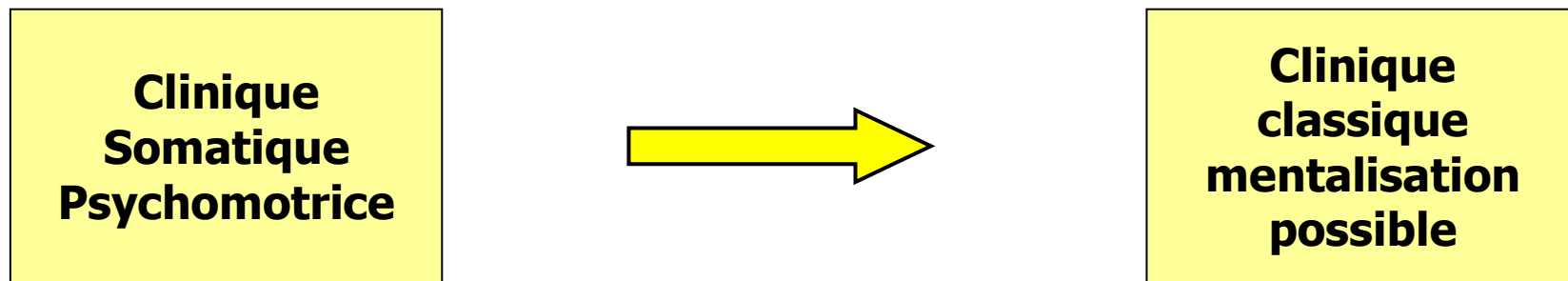
Same results in the study of offsprings of Amish Bipolar parents

Shaw et al, JAACAP, 2005

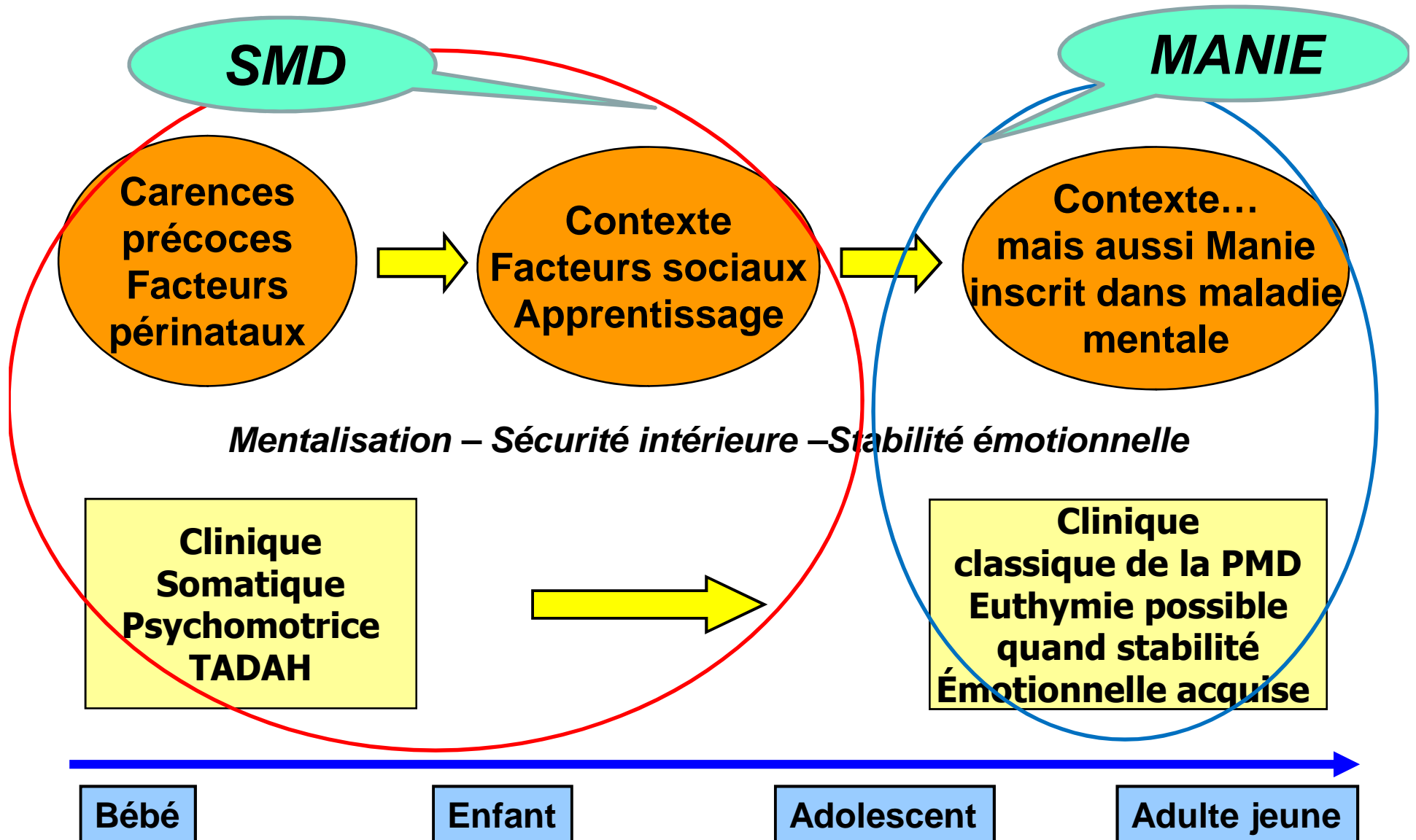
Une vue développementale de la dépression de l'enfant et de l'adolescent



Mentalisation – Morale – Estime de soi - Doute existentielle



Une vue développementale de l'hyperthymie de l'enfant et de l'adolescent



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Revue des études de devenir

(i) Critères étroits

	N	Age / Type de TB	Durée suivi	Stabilité diagnostique	≥ 1 rechute
Strober et al, 1995	54	Adolescents TB I	5 ans	100 %	44 %
Carlson et al, 2000	23	Adolescents TB I	2 ans	TB I: 82 % Schizophrénie, tr humeur pharmaco induit: 18 %	65 %
Jairam et al, 2004	25	Adolescents TB I	4 ans	100 %	64 %
Delbello et al, 2007	71	Adolescents TB I	1 an	100 %	50 %
Stingaridis et al, 2010	93	Adolescent TBI	2 ans		62,4%
Pitié (en cours)	80	Adolescents TB I	5 ans	TB I: 62 % Schizophrénie, schizo-aff : 38 %	91 %

Revue des études de devenir (ii) Critères larges

	N	Age / Type de TB	Durée du suivi	Stabilité diagnostique	≥ 1 rechute
COBY Birmaher et al, 2006	263	Enfants, adolescents TB I, II, nos	2 ans	100 %	50 %
Geller et al, 2008	115	Enfants, adolescents TB I, II, nos	8 ans	100 %	73 % (maniaque)
Stingaris et al, 2010	84	SMD	2 ans		1,3%

COBY STUDY

413 jeunes (7-17 ans) bipolaires large spectre suivis 4ans

FIGURE 1. Survival Analysis of Recovery From Index Episode in Youths With Bipolar Disorder, by Bipolar Subtype^a

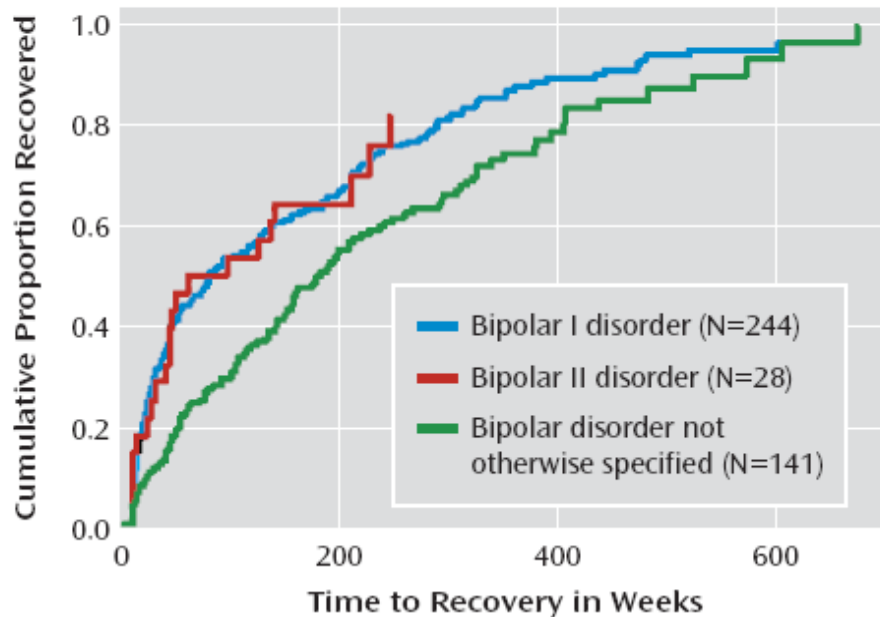
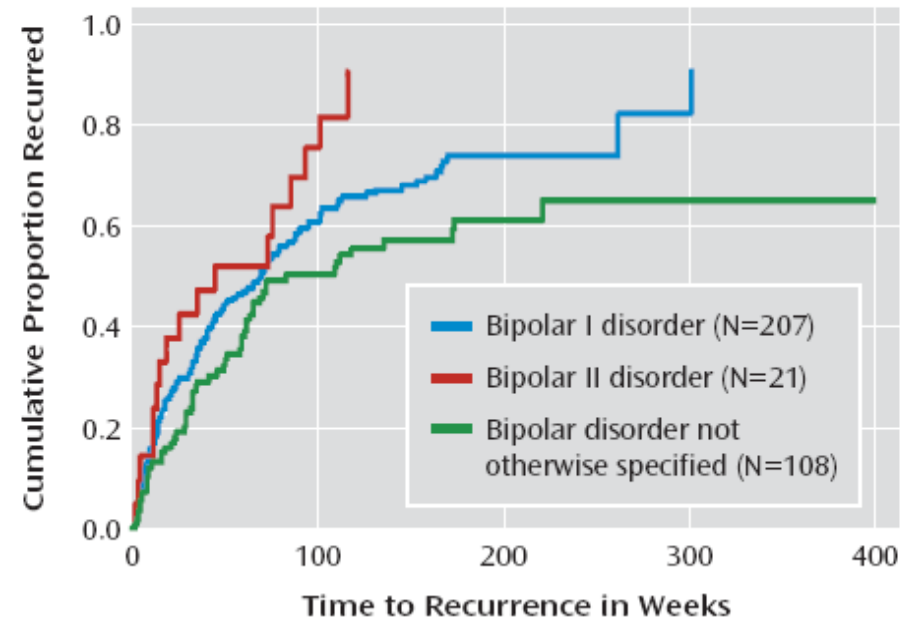


FIGURE 2. Survival Analysis of Recurrence After Recovery From Index Episode of Bipolar Disorder, by Bipolar Subtype^a



BIP I réponse au traitement mais également rechute plus rapide que BIP NOS

Birmaher et al, Am J Psy, 2009

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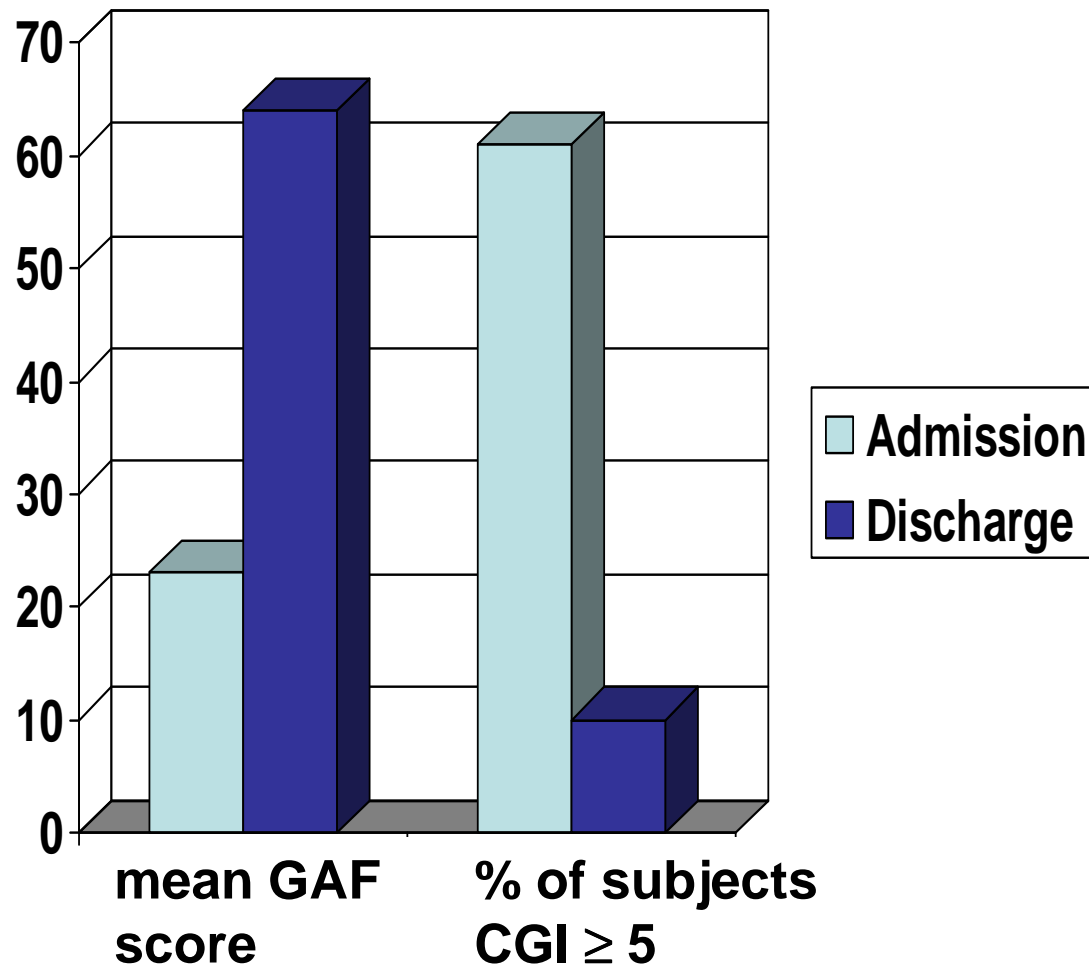
BIPOLAR DISORDER IN ADOLESENTS: INDEX EPISODE (N=80)

<p>Caractéristiques socio-demo</p> <p>Sexe</p> <p>Age (moyenne \pm SD) [min-max]</p> <p>SES: N (%) élevé et moyen</p> <p>Origine paternelle: N (%) migrants</p> <p>Origine maternelle: N (%) migrants</p>	<p>45 F, 35 M</p> <p>15.67 \pm 1.89 [12-20]</p> <p>50 (63.3)</p> <p>34 (44.2)</p> <p>33 (43.4)</p>
<p>ATCD</p> <p>ATCD perso: N (%)</p> <p>ATCD familiaux: N (%)</p> <p>Total IQ ^a (mean \pm SD)</p> <p>Verbal IQ ^b (mean \pm SD)</p> <p>Performance IQ ^c (mean \pm SD)</p>	<p>70 (87.5)</p> <p>51 (63.8)</p> <p>83.4 \pm 23.4</p> <p>89.94 \pm 22.2</p> <p>83.9 \pm 24.8</p>

BIPOLAR DISORDER IN ADOLESENTS: INDEX EPISODE (N=80)

<p>Caractéristiques cliniques</p> <p>Episode actuel</p> <p>Début brutal (≤ 10 jours): N (%)</p> <p>Traits Psychotiques : N (%)</p> <p>Traits Catatoniques : N (%)</p> <p>Retard mental : N (%)</p> <p>Durée séjour, (moyenne \pm SD) [min-max]</p>	<p>50 Maniac, 30 Mixed</p> <p>29 (36.3)</p> <p>51 (63.8)</p> <p>4 (5)</p> <p>17 (21.3)</p> <p>80.4 \pm 50.7 [17-245]</p>
<p>Scores à l'entrée</p> <p>GAF (mean \pm SD) [range]</p> <p>CGI-S: N (%) severely and extremely ill</p> <p>BPRS (mean \pm SD) [range]</p> <p>YMRS (mean \pm SD) [range]</p> <p>MADRS (mean \pm SD) [range]</p>	<p>23 \pm 7.9 [10-40]</p> <p>61 (76.3)</p> <p>63.3 \pm 15.0 [39-96]</p> <p>22.2 \pm 6.5 [12-36]</p> <p>19.5 \pm 8.5 [7-51]</p>
<p>Scores à la sortie</p> <p>GAF (mean \pm SD) [range]</p> <p>CGI-I: very much improved N (%)</p> <p>much improved N (%)</p> <p>minimally improved N (%)</p>	<p>64 \pm 14.4 [30-90]</p> <p>18 (22.4)</p> <p>51 (63,8)</p> <p>11 (13.8)</p>

BIPOLAR DISORDER IN ADOLESCENTS: INDEX EPISODE (N=80)



- Severe impairment
- N=50 (62.5%) psychotic features
- Duration of stay (mean=80.4 days)
- 86% very much or much improved at discharge

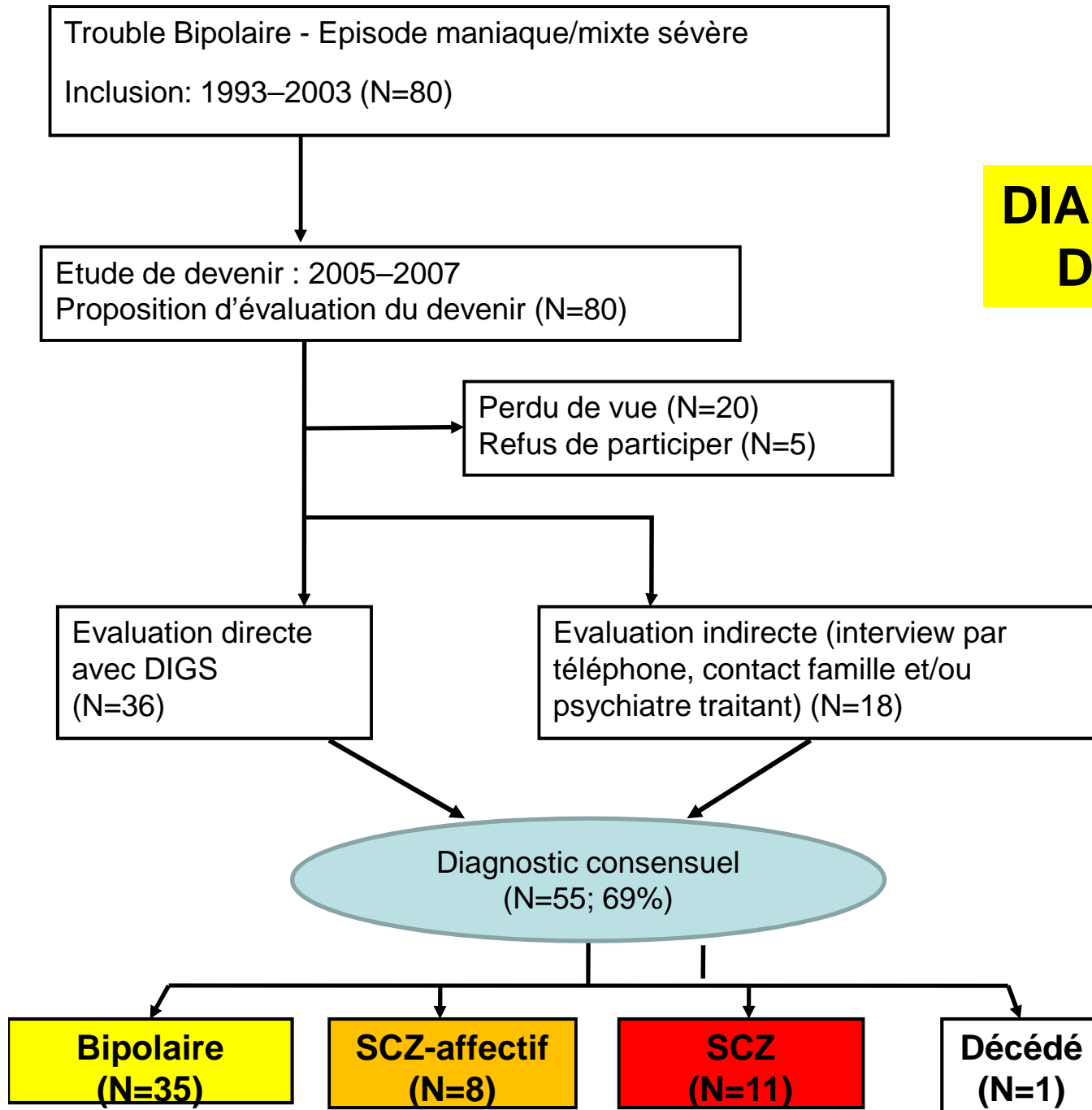
More manic than mixed in:

- subjects with MR
- subjects from migrant and/or low SES families

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DIAGRAM FLOW DE L'ETUDE



TROUBLE BIPOLAIRE TYPE 1: MORBIDITE ET MORTALITE AU FOLLOW-UP : ROW DATA

Au F/U: en moyenne 5 ans après [range: 2-10 years]

Mortalité et morbidité sont sévères avec un jeune qui est décédé d'un arrêt cardiaque, et 91% patients qui ont fait au moins une rechute.

Les patients sans rechute (N=5) et les patients qui ont un bon fonctionnement social (N=19) restent avec un diagnostic vie entière de BD I

Comorbidité développementale: Retard Mental (N=9), Autism (N=2)

FACTEURS DE RISQUES MEDICAUX ET DEVELOPPEMENTAUX CHEZ LES JEUNES HOSPITALISES POUR CATATONIE OU ETAT MANIAQUE

	Catatonia N=58	Bipolar Dis. N=80	X²	p
Organicity	13 (23%)	1 (1,3%)	17,57	<0.001
Developmental history	17 (30,9%)	17 (21,3%)	1.61	0.2

Catatonia: Prospective study; N=58; 1993 – 2010

Bipolar Disorder I: Follow-up study; N=80; 1993-2003; Mean FU= 4 years

FACTEURS ASSOCIES A UNE MEILLIEURE INSERTION SOCIALE (ICG: 1=Top – 7=Cata)

Variables étudiées: sexe, age index, age début, origine, SES, type index, psychose index, Cata index, tests psycho index, ATCD fam, durée index, abus toxiques, traitement, RM, insight, evenements, echelles index

Variable	CGI-Insertion score		Univariate
	Non	Oui	
SES	3.75	3.4	$p=0.08$
Test psycho ICG risque social	$\rho=-0.36$		$p=0.08$
NLP typiques	3.13	4.71	$p=0.001$
APA	3.14	4.33	$p=0.02$
RM	3.32	4.85	$p=0.003$
INSIGHT	5.08	3.32	$p=0.0003$

FACTEURS ASSOCIES A UNE MEILLIEURE INSERTION SOCIALE (ICG: 1=Top – 7=Cata)

Variables étudiées: sexe, age index, age début, origine, SES, type index, psychose index, Cata index, tests psycho index, ATCD fam, durée index, abus toxiques, traitement, RM, insight, evenements (perte, abus sexuel, maltraitance), echelles index

Variable	CGI-Insertion score		Univariate
EGF	$\rho = -0.89$		$p < 0.001$
CGI-S	$\rho = 0.89$		$p < 0.001$
BPRS	$\rho = 0.77$		$p < 0.001$
YMRS	$\rho = 0.67$		$p < 0.001$
MADRS	$P = 0.58$		$p < 0.001$
Evts PERTE	2.25	3.85	$p = 0.09$
ABUS SEXUEL	3.34	4.8	$p = 0.049$

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FACTEURS ASSOCIES A UNE TRANSITION DIAGNOSTIQUES VERS LE SPECTRE SCZ

Variables étudiées: sexe, age index, age début, origine, SES, type index, psychose index, Cata index, tests psycho index, ATCD fam, durée index, abus toxiques, traitement, RM, insight, evenements (perte, abus sexuel, maltraitance), echelles index

Variable	Diagnosis at follow-up		Univariate
	BD I	SCZ-affect or SCZ	
CGI-S	2.95	4.82	<i>p=0.004</i>
EGF	67	43.8	<i>p=0.003</i>
BPRS	29.52	40	<i>p=0.034</i>
YMRS	3.81	4.78	<i>p=0.063</i>
MADRS	3.71	7.11	<i>p=0.053</i>
SAS/ICG-inser	1.47	2.8	<i>p=0.024</i>

FACTEURS ASSOCIES A UNE TRANSITION DIAGNOSTIQUES VERS LE SPECTRE SCZ

Variables étudiées: sexe, age index, age début, origine, SES, type index, psychose index, Cata index, tests psycho index, ATCD fam, durée index, abus toxiques, traitement, RM, insight, evenements (perte, abus sexuel, maltraitance), echelles index

Variable	Diagnosis at follow-up		Univariate
	BD I	SCZ-affect or SCZ	
Test psycho ICG risque social	2.54	1.6	<i>p=0.051</i>
Test psycho ICG risque SCZ	2.91	2.15	<i>p=0.087</i>
APA	Plus d'APA chez les SCZ		<i>p=0.0037</i>
THYMOREG	Plus de THYMOREG chez les BIP		<i>p=0.05</i>

FACTEURS ASSOCIES AUX RECHUTES

Variables étudiées: sexe, age index, age début, origine, SES, type index, psychose index, Cata index, tests psycho index, ATCD fam, durée index, abus toxiques, traitement, RM, insight, evenements (perte, abus sexuel, maltraitance), echelles index

Variable	Coeff de corrélation		Univariate
EGF	$\rho = -0.54$		<i>p=0.004</i>
CGI-S	$\rho = 0.45$		<i>p=0.023</i>
SAS/ICG-inser	$\rho = 0.62$		<i>p=0.004</i>
Test psycho ICG risque social	$\rho = -0.48$		<i>p=0.038</i>
Test psycho ICG risque SCZ	$\rho = -0.4$		<i>p=0.089</i>
Abus TOXIQUE			<i>p=0.05</i>
NLP typique			<i>p=0.003</i>

ICG – SCHIZOPHRENIA RISK

	TAT	RORSCHARCH
Processus de pensée	Perception, socialisation secondarisation, rapport pensée/fantasme	Perception (F+%↘), secondarisation, rapports pensée/ fantasme et peception/pensée
Qualité de l'image du corps	Malformations (E1) Confusion d'identité (E 3)	Image fragmentée (Hd>H, H morbides, Ad>A) Indifférenciation
Qualité du narcissisme	Représentations massives Thèmes mégalo (E), mort, anéantissement	Projection, toute puissance Défaillance de support, des enveloppes
Qualité de l'expression des affects	Affects massifs ou froideur, Cruidité de l'expression Hermétisme	Affects massifs ou = 0, Discordance affect /représentation Hermétismes, Emergences pulsionnelles
Qualité des relations objectales	Relation destructrice et/ou persécutive, et fusionnelle Identification projective Omnipotence	Destructivité, Identification project, Absence d'investissement objectal (pas de K, pas de représentations de relations), Dédoublment



Inter-rater reliability, $N_1=16$ tests, $N_2=3$ raters

intraclass corr=0.74, Kappa=0.74

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CONCLUSION

<i>Symptômes maniaques de l'enfant</i>	<i>Episodes maniaques de l'adolescent</i>
Chronique et continu	Episodique
Comorbidité élevée au TDAH	ATCDs de TDAH marginaux
Symptômes psychotiques exceptionnels	30 à 60% de symptômes psychotiques
ATCDs familiaux très variés	ATCDs familiaux de bipolarité
Facteurs environnementaux au premier plan et troubles des apprentissages fréquents	Fonctionnement prémorbide souvent de bonne qualité

