Difficultés psychiques associées à la microdélétion22

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Plan

- Introduction
- Les difficultés les plus fréquentes en fonction de l'âge
- Sévérité et intensité des symptômes psychotiques
- Discussion et QUESTIONS/REPONSES

Introduction

- Les difficultés psychiques et la maladie psychiatrique sont sources de grande anxiété chez les proches et les personnes avec Del22q11
- Une partie de cette anxiété n'est pas rationelle et souvent liée à un manque de connaissance
- Quand les difficultés surviennent, il est nécessaire de les comprendre pour pouvoir agir efficacement
- LES MALADIES PSYCHIATRIQUES GRAVES SONT RARES. La majorité des personnes ne sont pas affectées.
- Il existe des traitements pour réduire les symptômes ou traiter les troubles psychiatriques

Problèmes psychiatriques les plus fréquents chez les enfants et adultes avec une microdélétion 22q11

Méthode

- 73 enfants et adultes avec microdélétion 22q11 qui ont spontanément pris contact avec notre équipe pour une évaluation à Genève
- Toutes les personnes évaluées par Stephan Eliez sur la base d'un entretien avec les parents et l'enfant/adulte.
- DICA+K-SADS pour les enfants, SCID et SADS pour les adultes

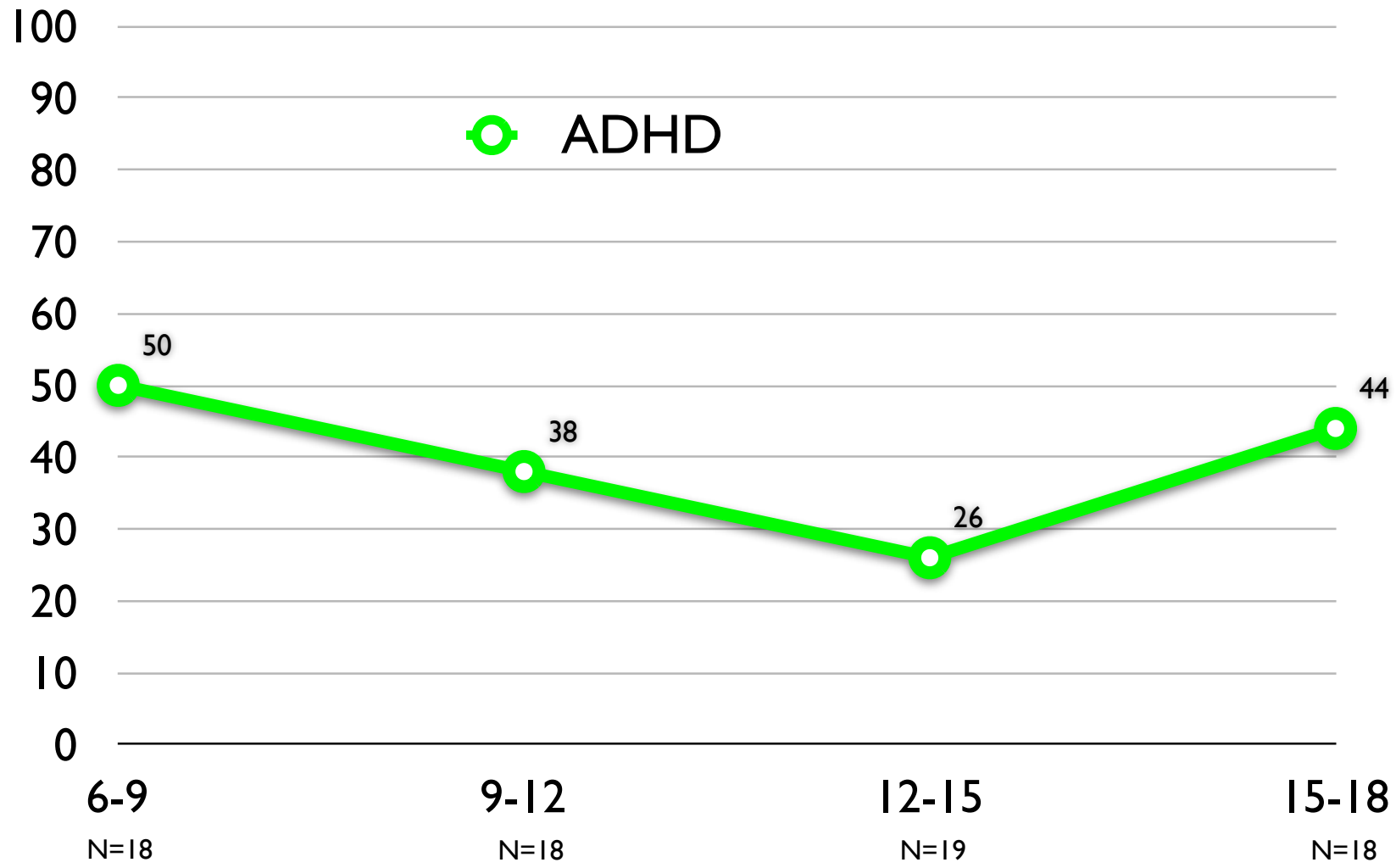
Psychiatric Disorders and Intellectual Functioning Throughout Development in Velocardiofacial (22q11.2 Deletion) Syndrome

TAMAR GREEN, M.D., DORON GOTHELF, M.D., BRONWYN GLASER, PH.D., MARTIN DEBBANE, PH.D., AMOS FRISCH, PH.D., MOSHE KOTLER, M.D., ABRAHAM WEIZMAN, M.D., AND STEPHAN ELIEZ, M.D.

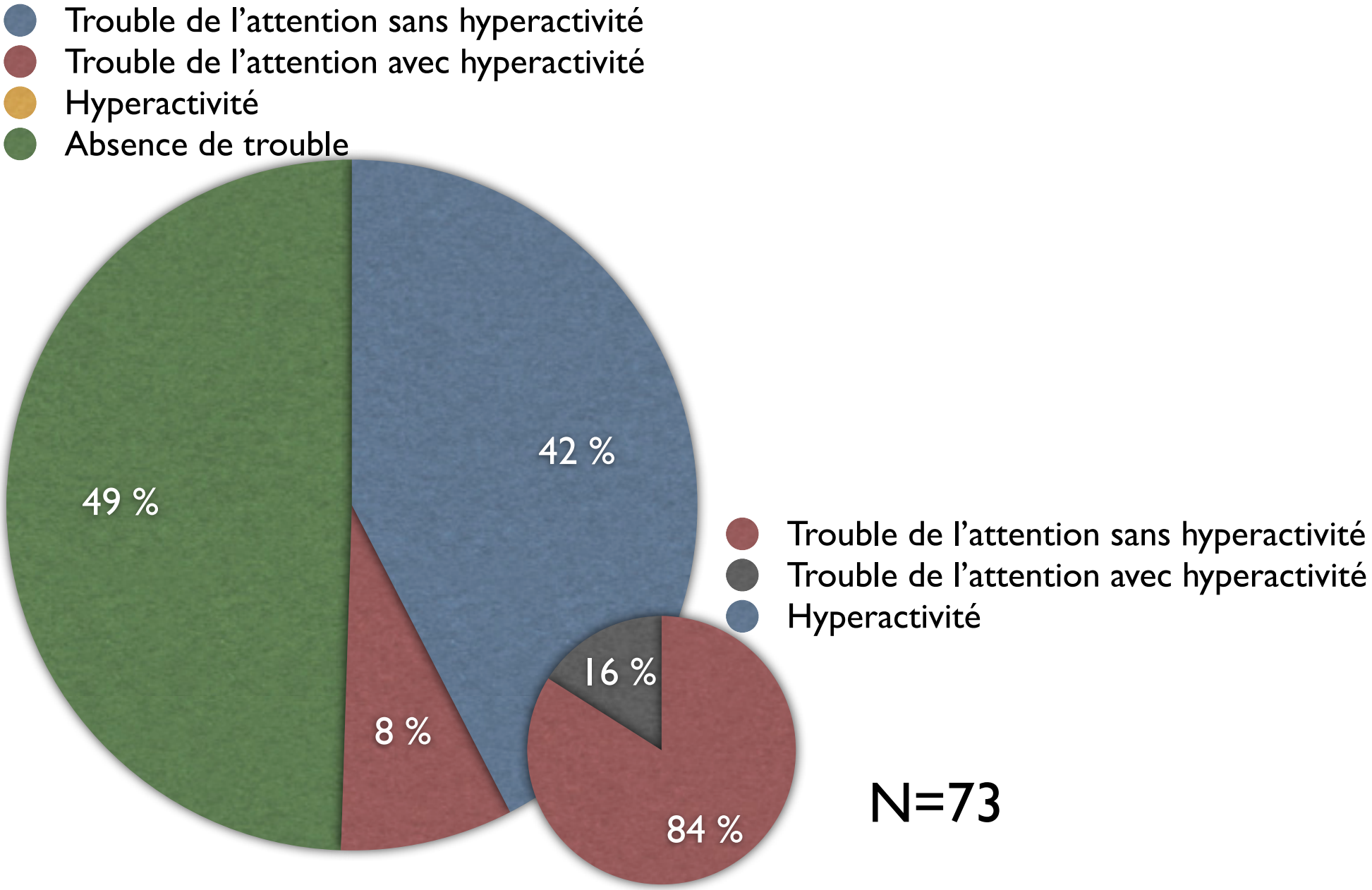
ABSTRACT

Objective: Velocardiofacial syndrome (VCFS) is associated with cognitive deficits and high rates of schizophrenia and other neuropsychiatric disorders. We report the data from two large cohorts of individuals with VCFS from Israel and Western Europe to characterize the neuropsychiatric phenotype from childhood to adulthood in a large sample. **Method:** Individuals with VCFS (n = 172) aged 5 to 54 years were evaluated with structured clinical interviews for psychiatric disorders and age-appropriate versions of the Wechsler intelligence tests. **Results:** The frequency of psychiatric disorders was high and remarkably similar between samples. Psychotic disorders and depression were uncommon during childhood but increased in rates during adulthood (depressive disorders: 40.7% in young adults [aged 18–24 years]; psychotic disorders: 32.1% in adults [age >24 years]). Cognitive scores were inversely associated with age in subjects with VCFS, including patients without psychosis. Specifically, Verbal IQ (VIQ) scores negatively correlated with age, and the subjects with VCFS and psychotic disorders had significantly lower VIQ scores than nonpsychotic VCFS subjects. **Conclusions:** Neuropsychiatric deficits in individuals with VCFS seem to follow a developmental pattern. The VIQ scores are negatively associated with age and rates of mood, and psychotic disorders increase dramatically during young adulthood. The data presented here support careful monitoring of psychiatric symptoms during adolescence and young adulthood in VCFS. Prospective longitudinal studies are needed to examine the nature of age-related cognitive changes and their association with psychiatric morbidity in VCFS. *J. Am. Acad. Child Adolesc. Psychiatry,* 2009;48(11):1060–1068. **Key Words:** 22q11.2 deletion syndrome, schizophrenia, Verbal IQ, depression mood disorders, neurodevelopmental disorder.

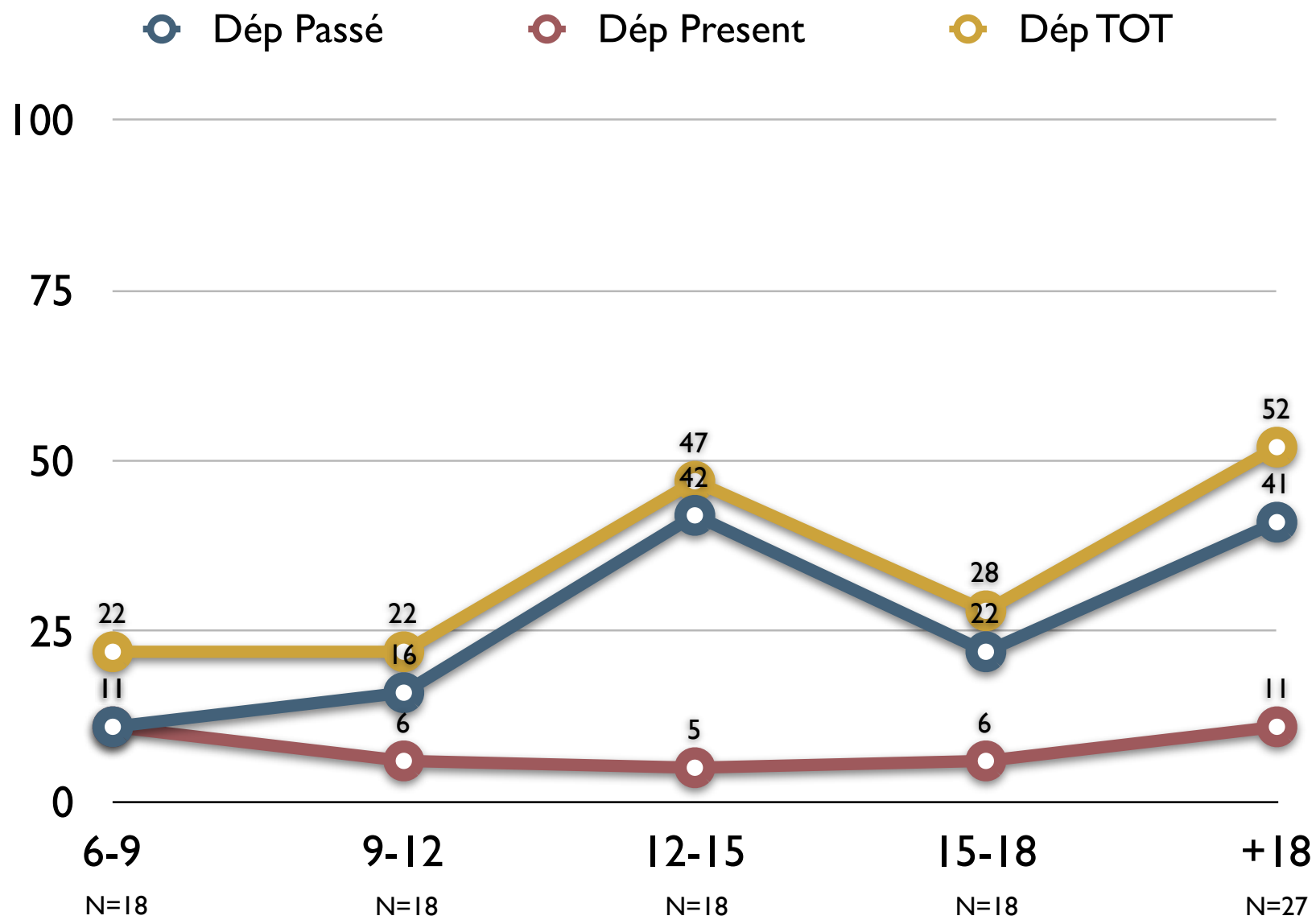
Trouble hyperactif et déficit de l'attention



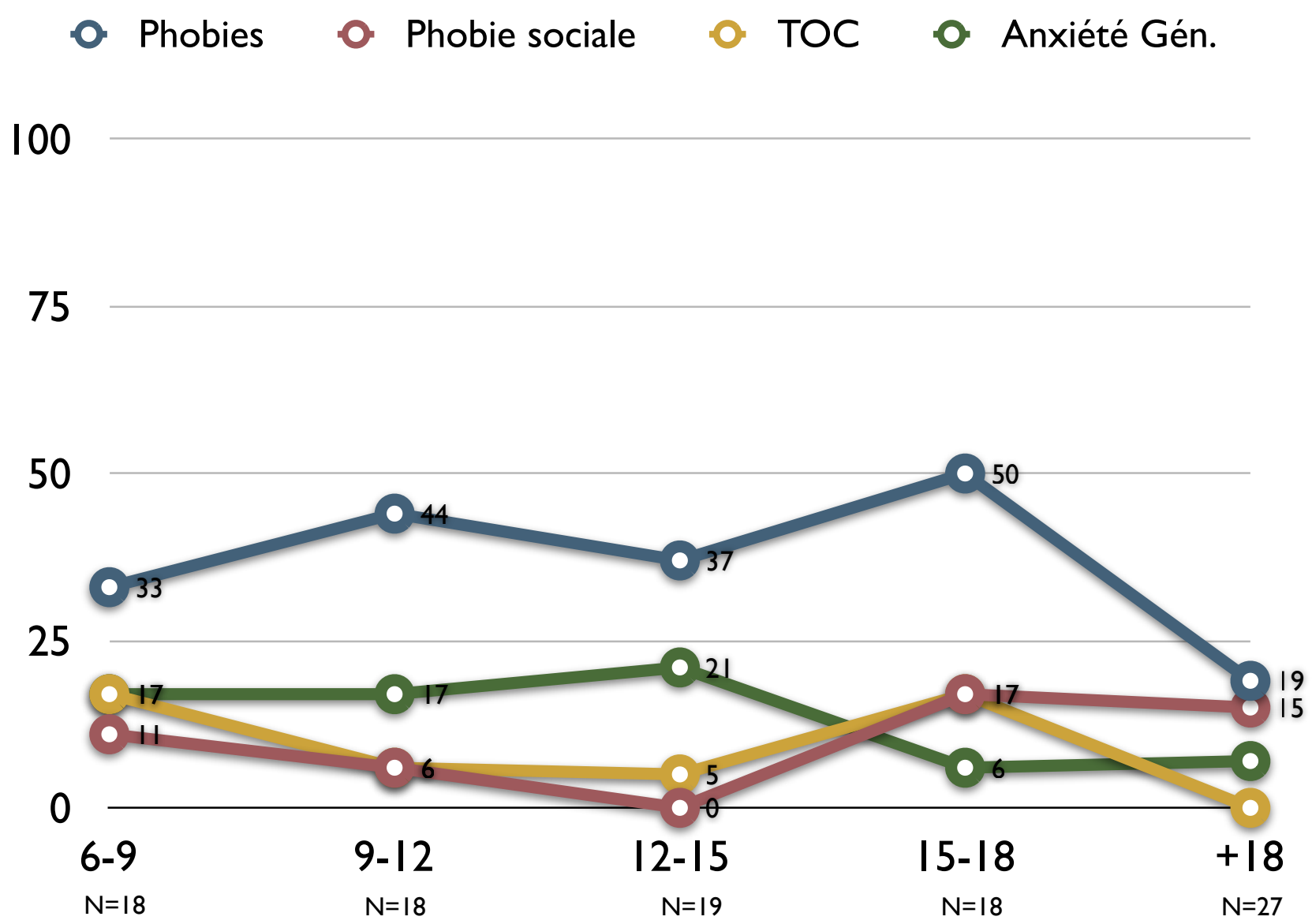
Types ADHD


Trouble de l'attention sans hyperactivité
Trouble de l'attention avec hyperactivité
Hyperactivité
Absence de trouble
42 %
49 %
8 %
16 %
84 %
Trouble de l'attention sans hyperactivité
Trouble de l'attention avec hyperactivité
Hyperactivité
N=73

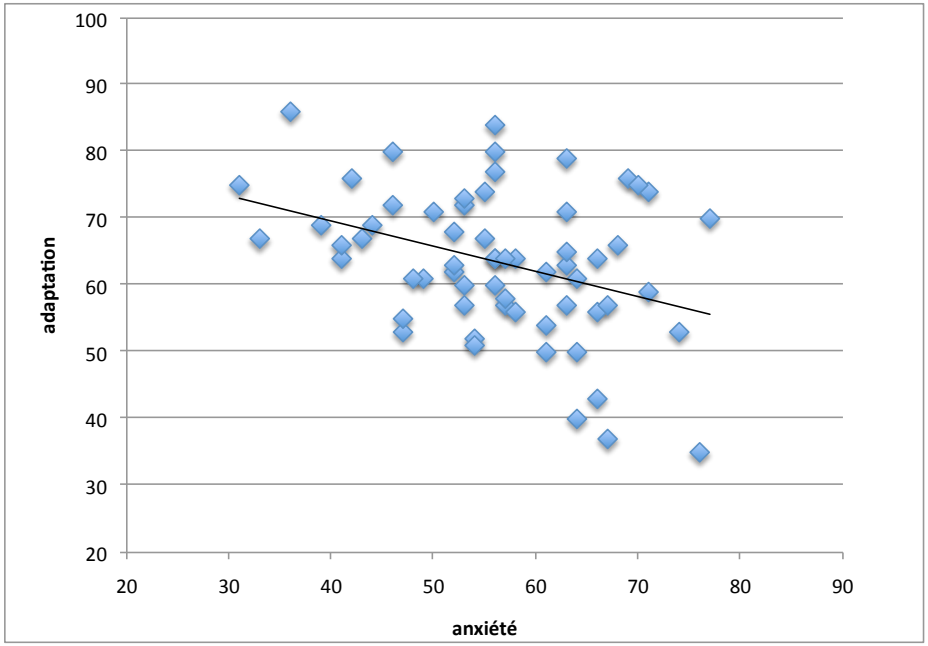
Dépression

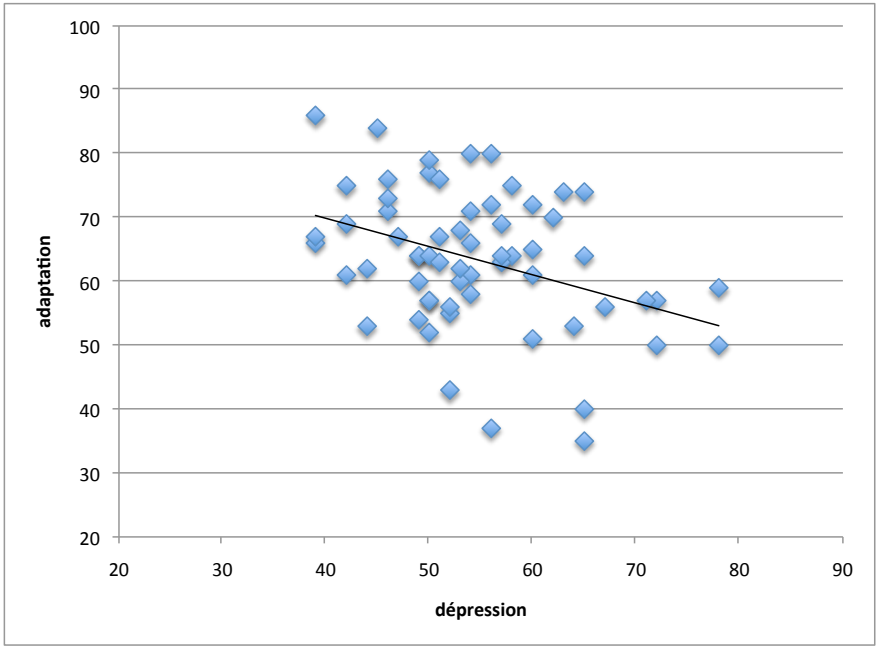

Dép Passé
Dép Present
Dép TOT
100
75
50
25
0
22
22
47
28
52
11
16
42
22
41
11
6
5
6
6-9
9-12
12-15
15-18
+18
N=18
N=18
N=18
N=18
N=27

Troubles psychiatriques

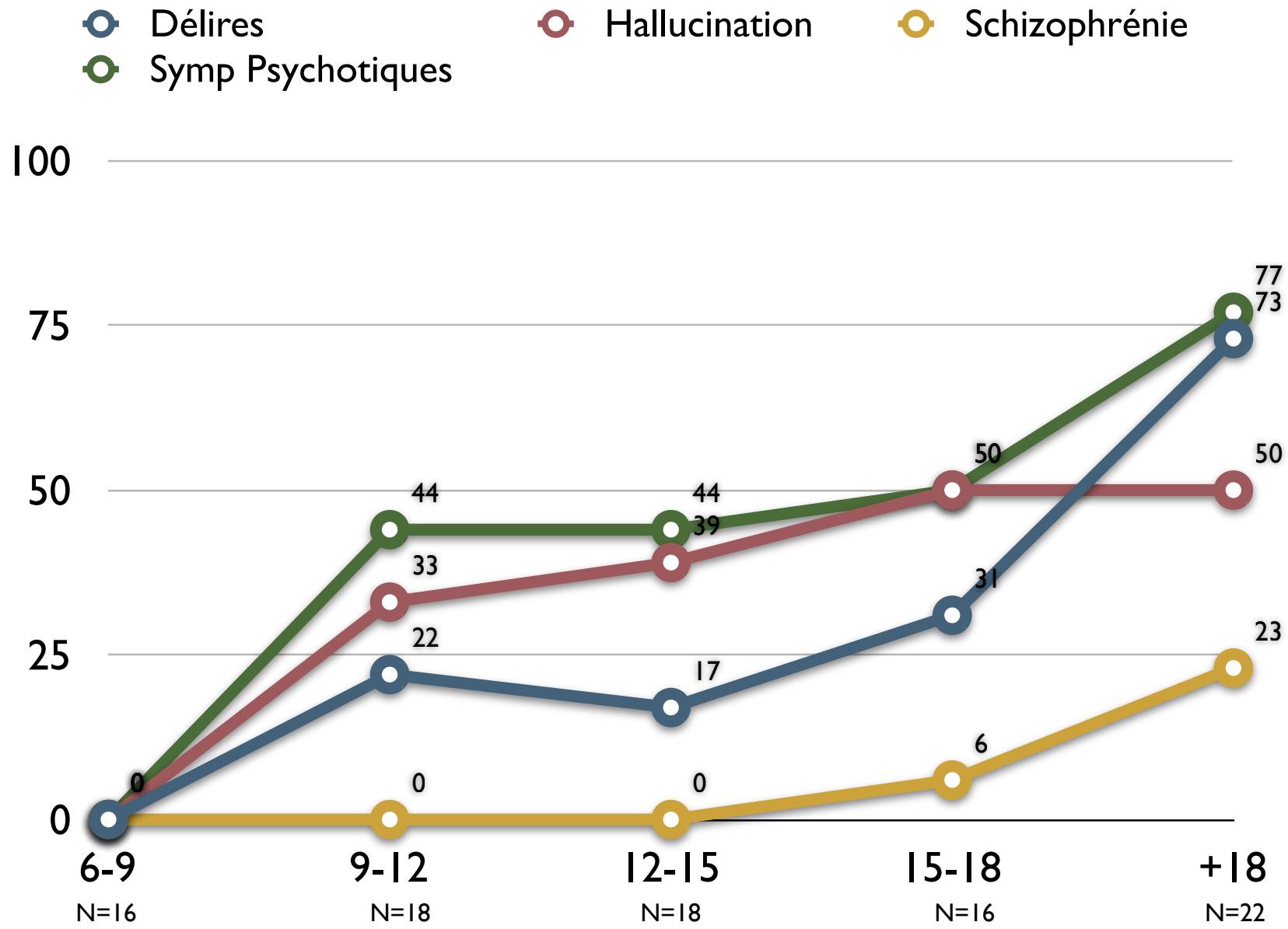


Troubles émotionnels et adaptation

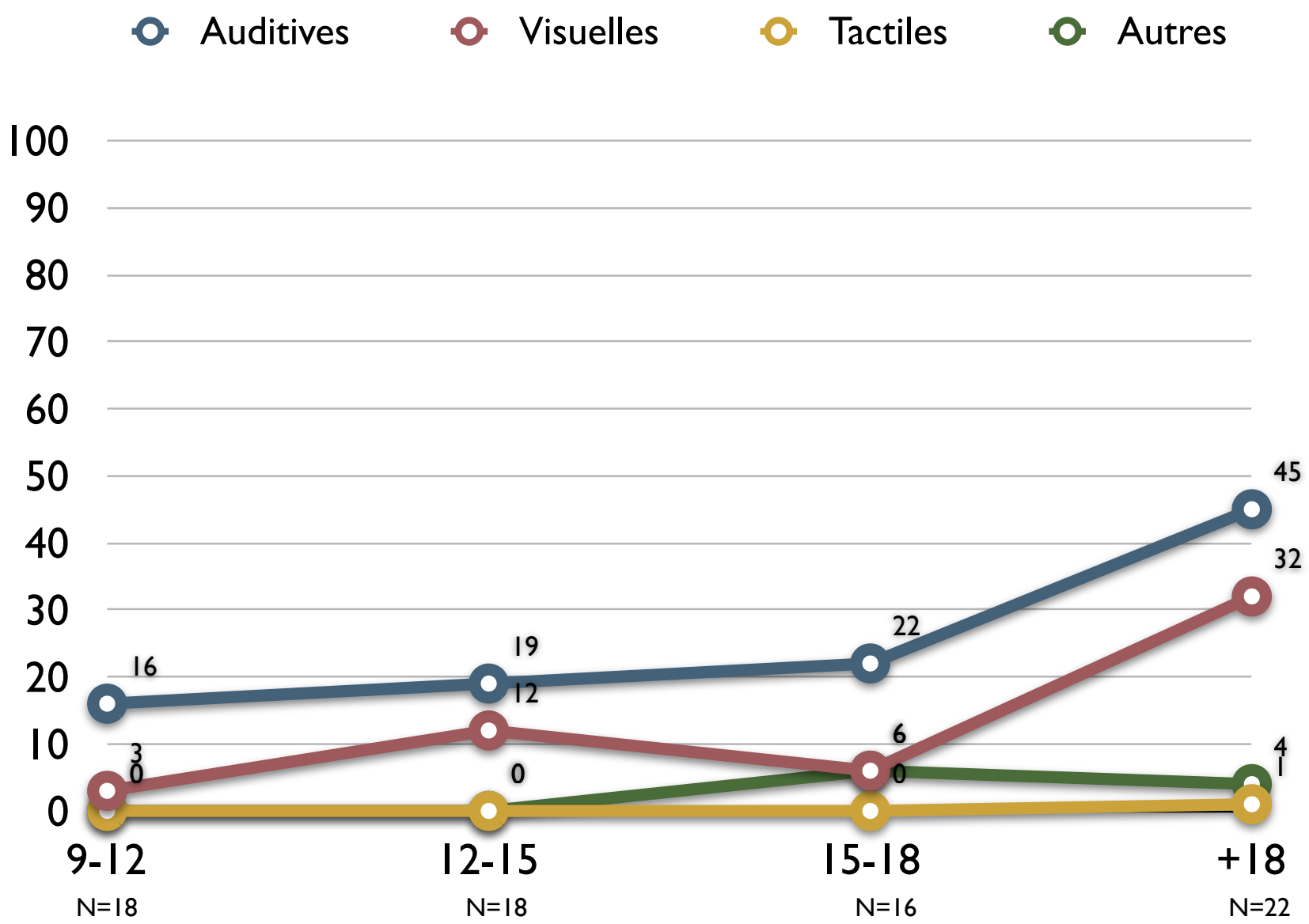




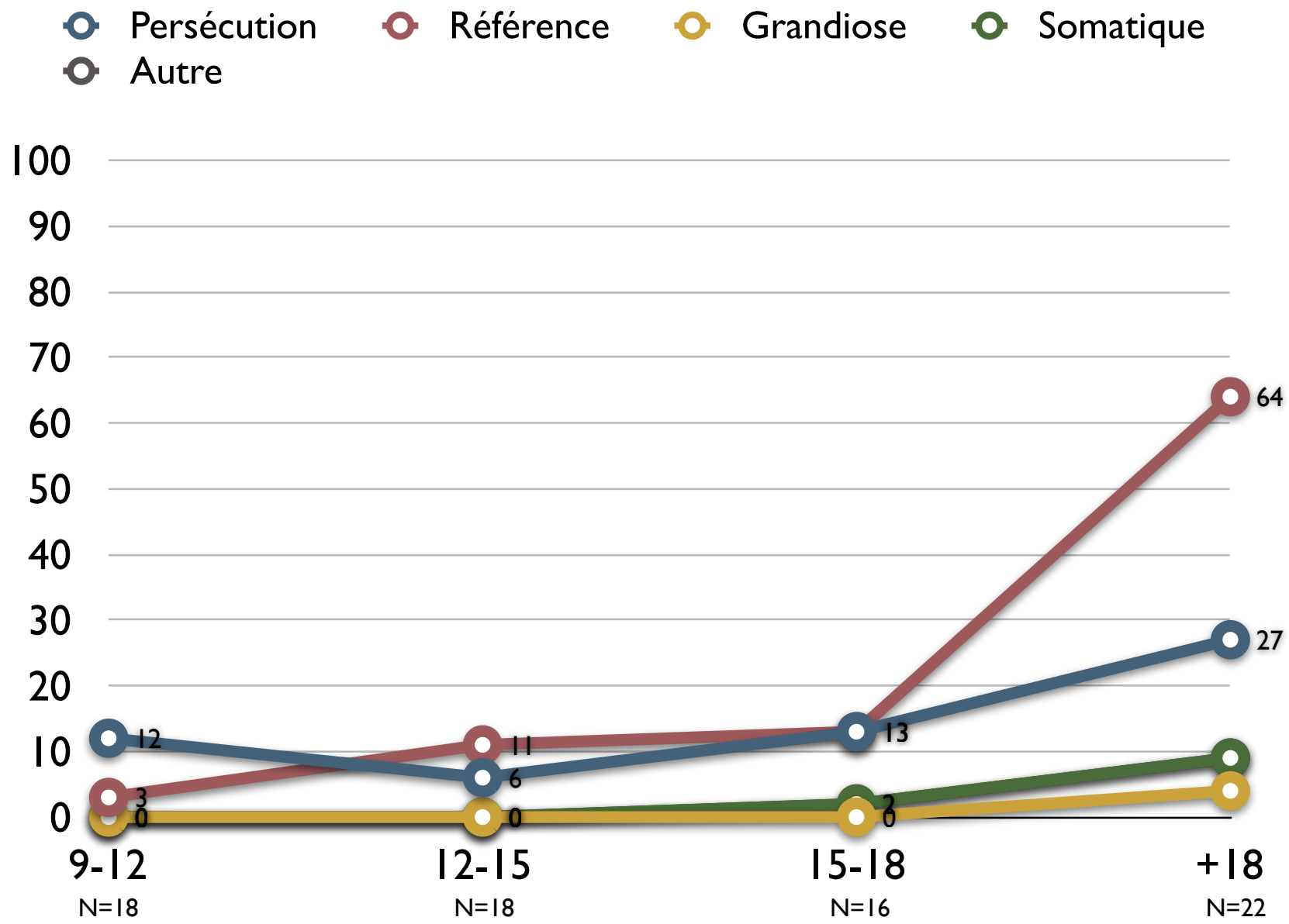
Fréquence des symptômes psychotiques



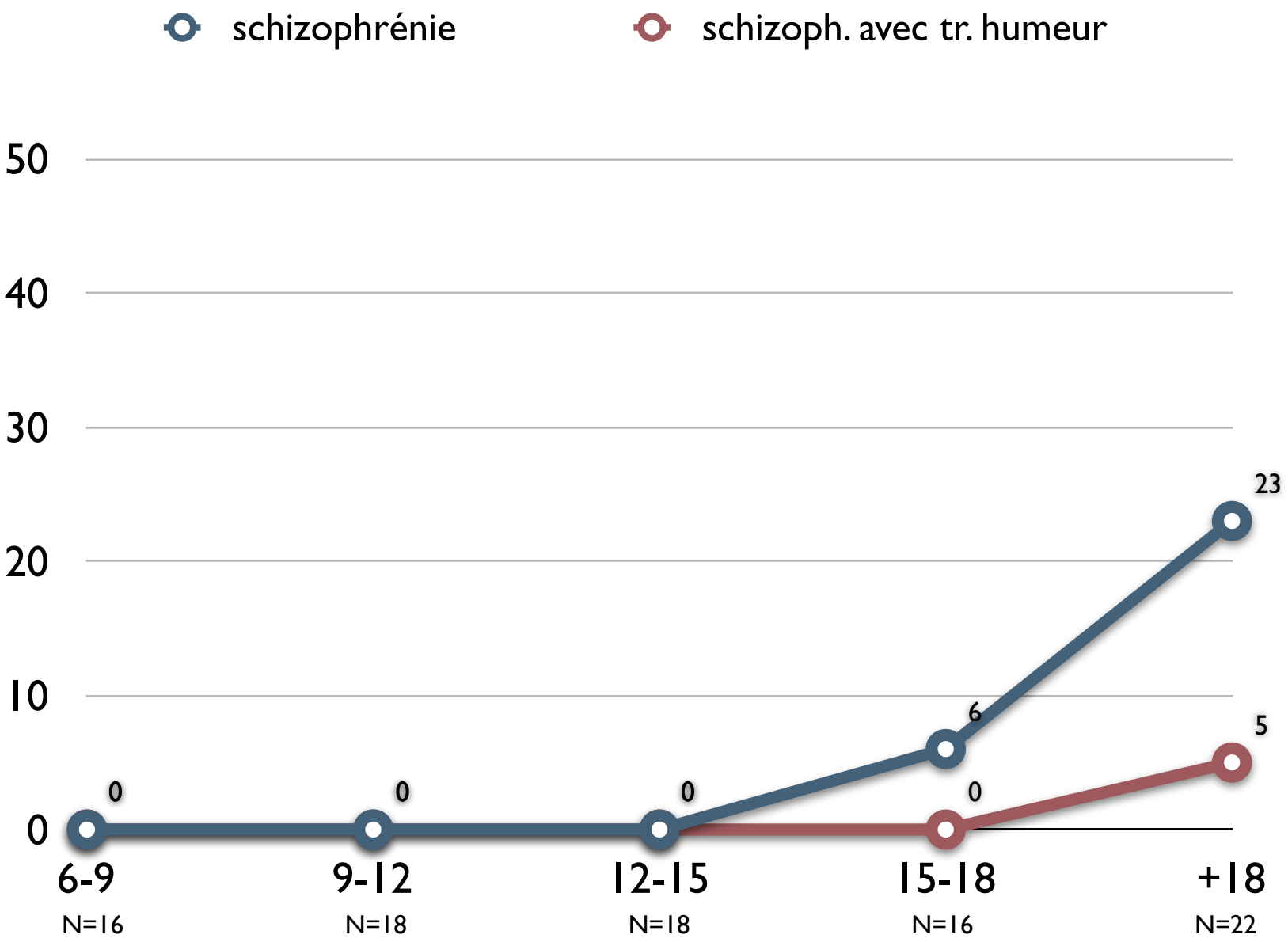
Type d'hallucinations

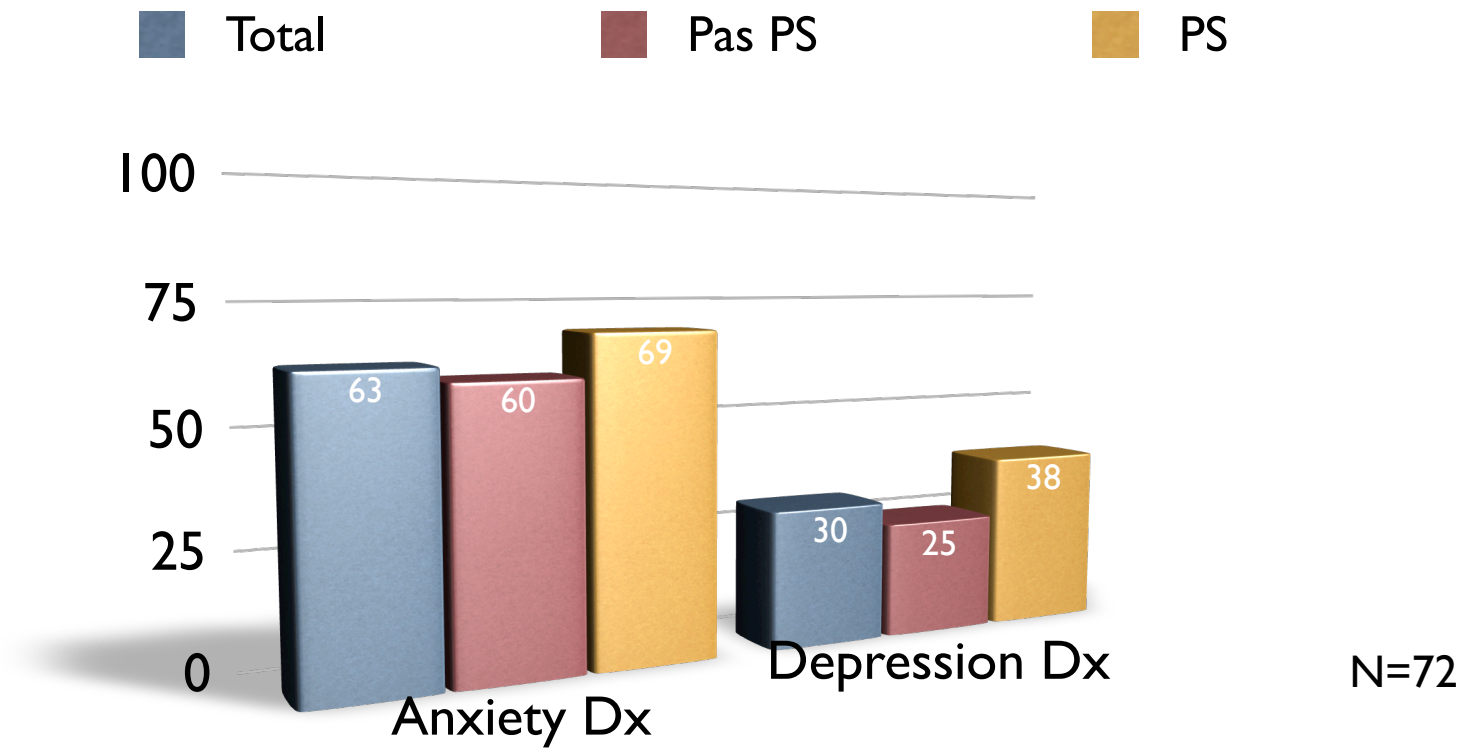


Types de délires



Schizophrénie





- Anxiété et dépression sont fréquents et important à repérer
- Lien avec la présence de symptômes positifs
- Importance d'une intervention précoce de ces difficultés

Structured Interview for Prodromal Syndromes - SIPS

Miller, T.J. et al. *Psychiatric Quarterly*, 1999

- 47 participants avec le syndrome VCFS évalués.
- sexe: 18 garçons, 29 filles
- âges:
  - moins 15 ans -->N=20
  - 15-18 ans -->N=15
  - 18+ -->N=12
  - âge moyenne = 16.6 ans
  - âge E-T = 4.8 ans
- Échelle de sévérité des symptômes de 1 (présence questionnable) – 6 (sévère et psychotique)

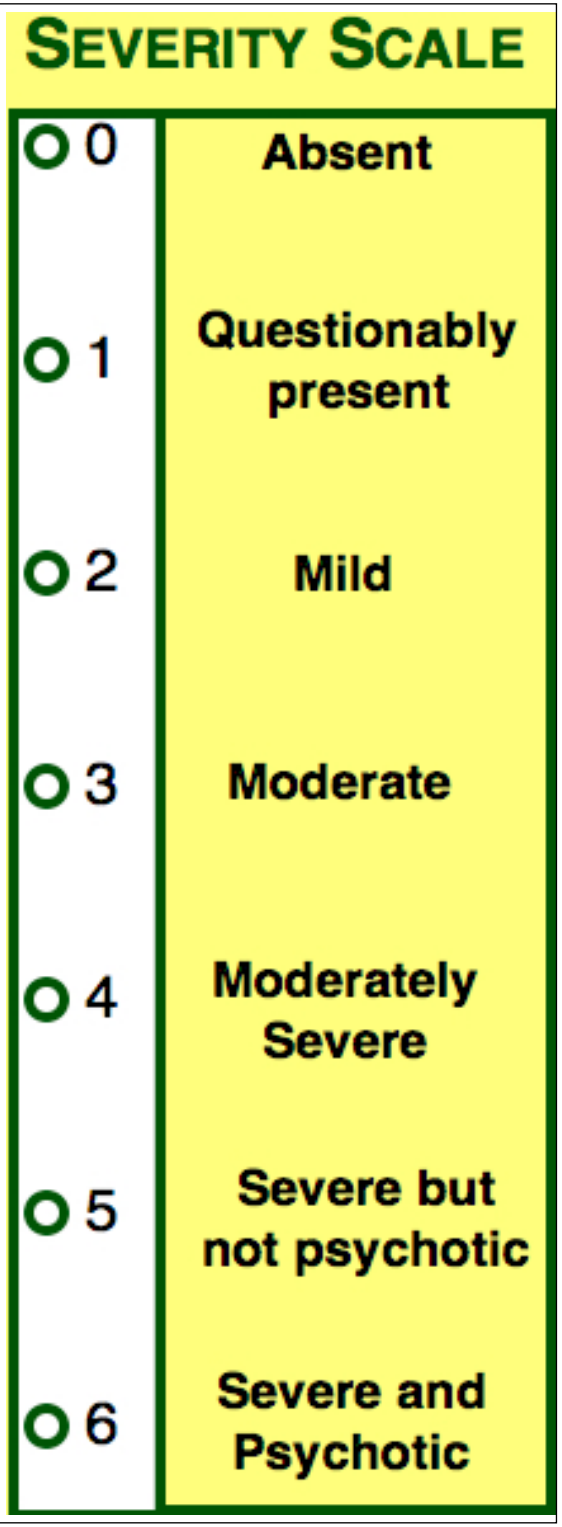
4 Dimensions

1. Symptômes Positifs

CONTENU INHABITUEL DE LA PENSÉE/IDEÉES DÉLIRANTES
MÉFIANCE/IDEES PERSÉCUTRICES
IDÉES GRANDIOSES
ANOMALIES PERCEPTIVES/HALLUCINATIONS
COMMUNICATION DÉSORGANISÉE

2. Symptômes Négatifs

ANHÉDONIE SOCIALE
AVOLITION
EXPRESSION DES ÉMOTIONS
EXPÉRIENCE DES ÉMOTIONS ET SELF
RICHESSE CONCEPTUELLE
FONCTIONNEMENT OCCUPATIONNEL



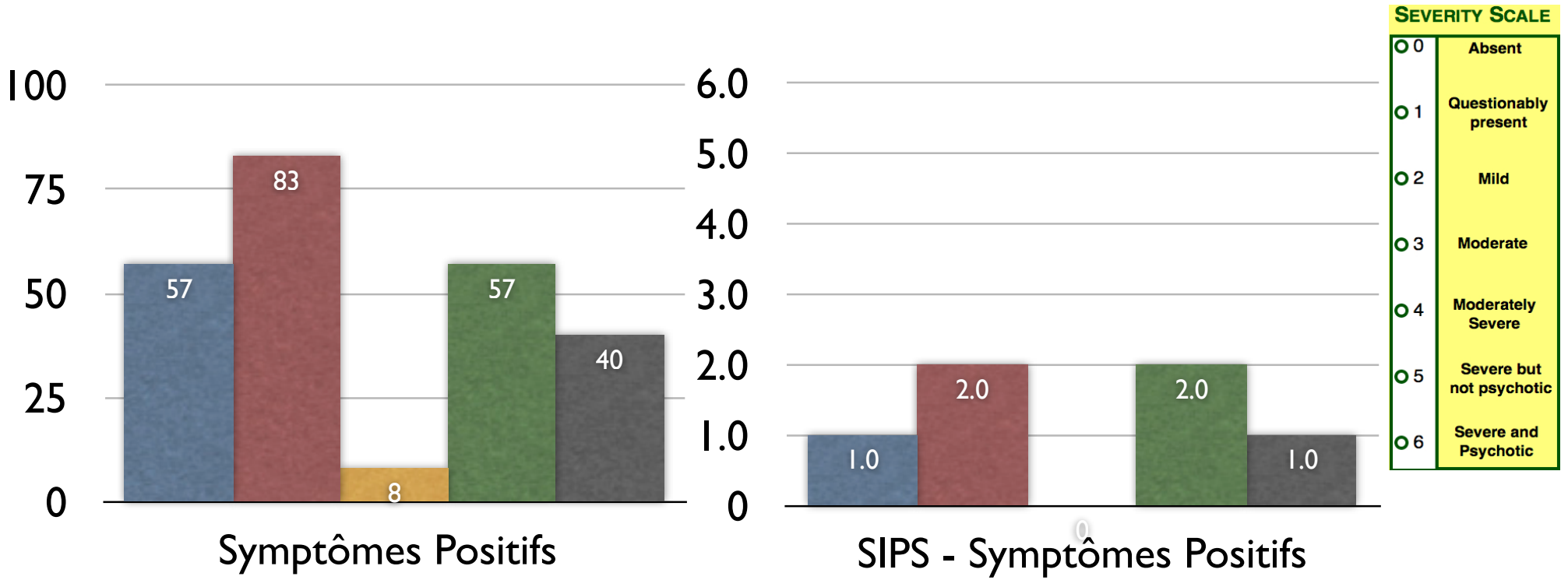
3. Symptômes de Désorganisation

COMPORTEMENT OU APPARENCE ÉTRANGE
PENSÉES BIZARRES
TROUBLE DE LA FOCALISATION ET DE L'ATTENTION
DÉGRADATION DANS L'HYGIÈNE PERSONNELLE

4. Symptômes Généraux

TROUBLES DU SOMMEIL
HUMEUR DYSPHORIQUE
DÉRANGEMENT MOTEUR
TOLÉRANCE AU STRESS NORMAL AFFAIBLIE

SEVERITY SCALE	
0	Absent
1	Questionably present
2	Mild
3	Moderate
4	Moderately Severe
5	Severe but not psychotic
6	Severe and Psychotic



Fréquence

Sévérité

- Unusual Thought Content / Delusional Ideas
- Suspiciousness / Persecutory Ideas
- Grandiose Ideas
- Perceptual Anomalies / Hallucinations
- Disorganized Communication

Auditives

1. Sentez-vous parfois que vos oreilles vous jouent des tours ? 19 %

2. Vous êtes-vous senti plus sensible aux sons ? 32 %

3. Vous arrive-t-il parfois d'entendre des bruits inhabituels comme des cognements, des claquements, des sifflements, des applaudissements, des sonneries dans vos oreilles ? 53 %

4. Vous arrive-t-il de penser que vous entendez des sons et réalisez ensuite qu'il n'y avait probablement rien ? 43 %

5. Entendez-vous parfois vos propres pensées comme si elles étaient racontées en dehors de votre tête ? 15 %

6. Vous arrive-t-il d'entendre une voix que les autres ne semblent pas entendre ou ne peuvent pas entendre ? 46 %

Visuelles

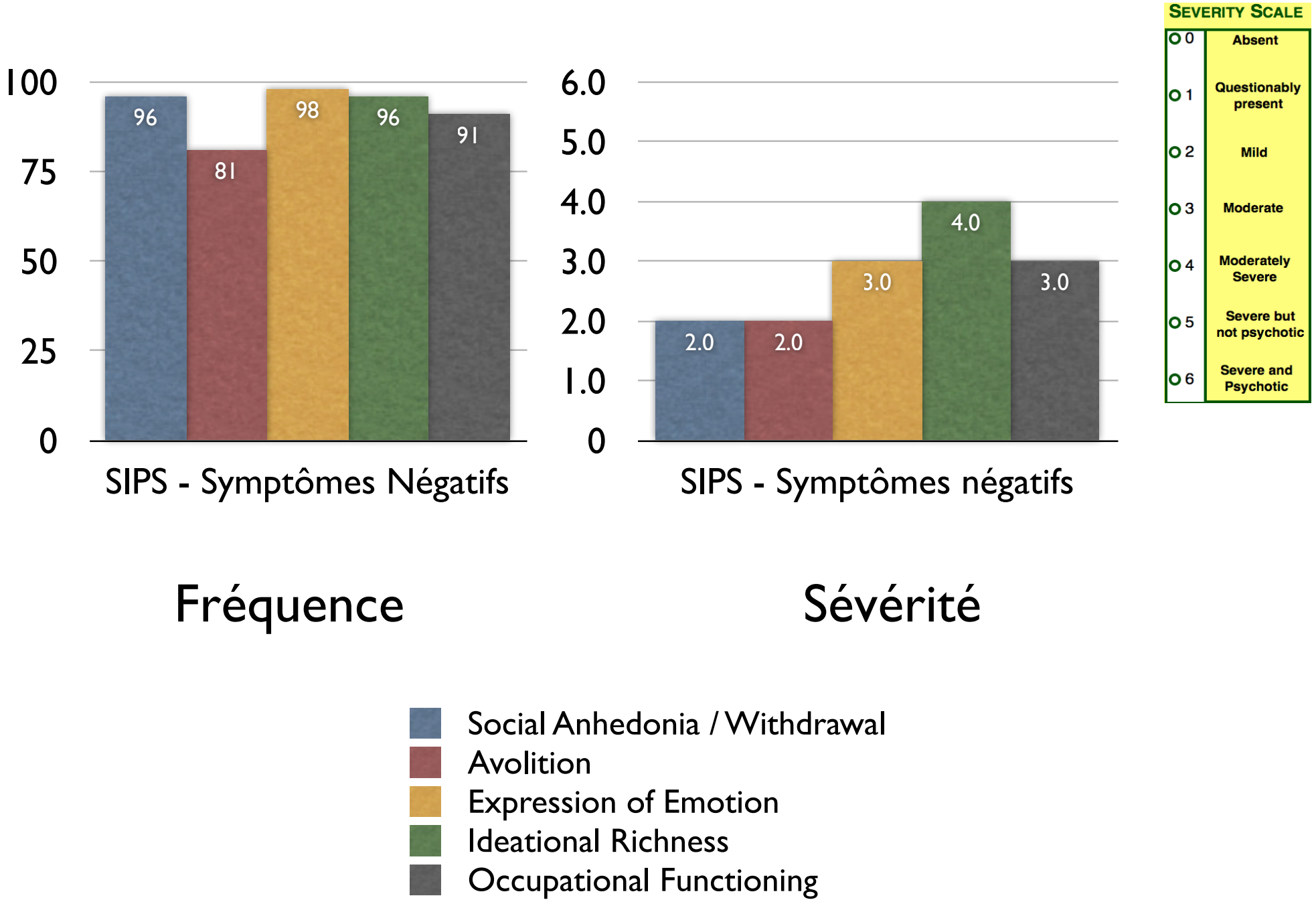
1. Vous arrive-t-il de sentir que vos yeux vous jouent des tours ? 15 %

2. Vous semble-t-il être plus sensible à la lumière ou faire des choses que vous voyez apparaître avec des différences de couleur, de luminosité, de clarté ou flou, ou qui ont changé d'une autre manière ? 8 %

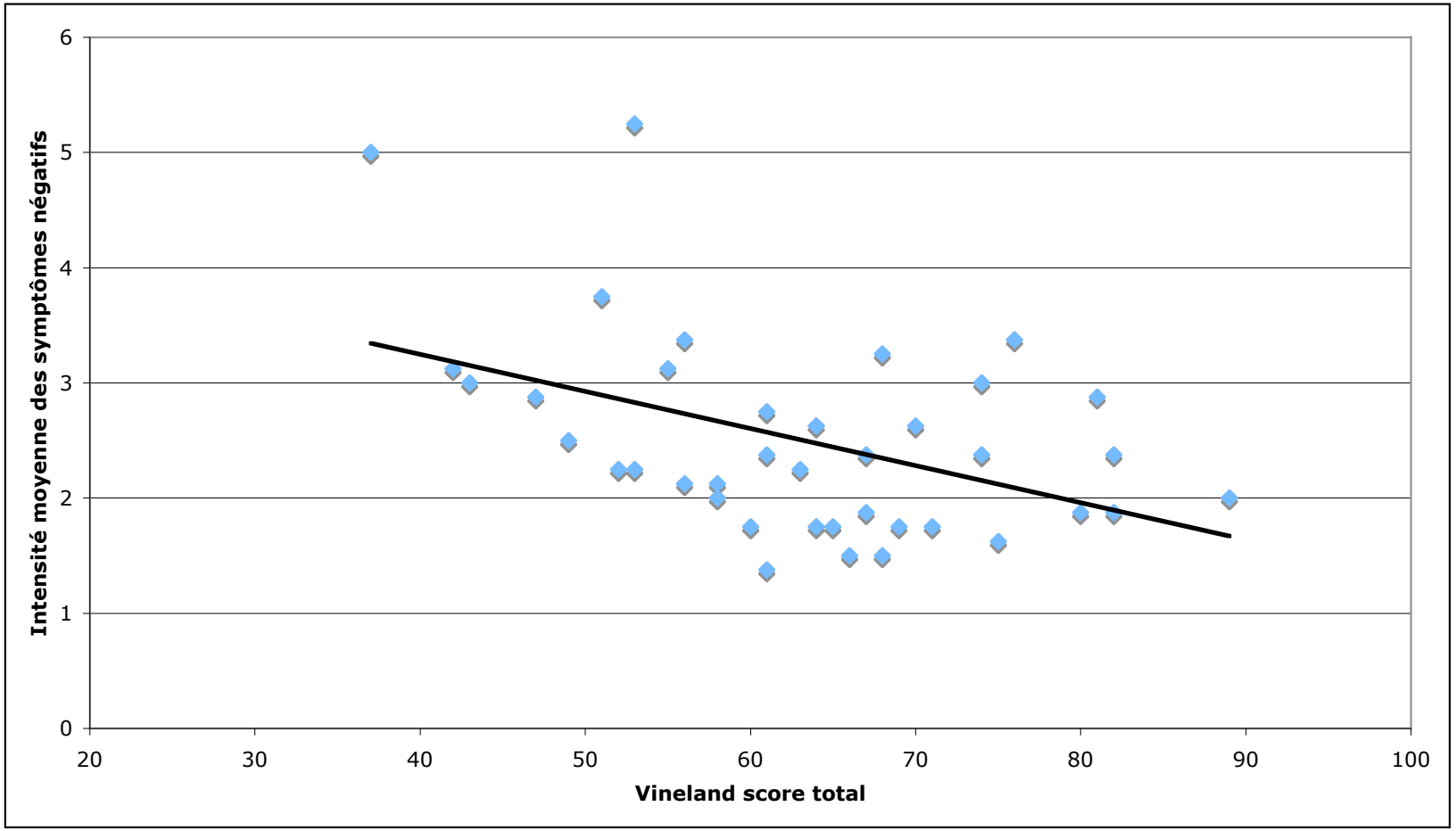
3. Avez-vous déjà vu des choses inhabituelles comme des flashs, des flammes, des figures vagues ou des ombres en dehors de votre coin d'œil ? 23 %

4. Vous arrive-t-il de penser voir des gens, animaux ou objets et ensuite réaliser qu'ils peuvent ne pas vraiment être là ? 17 %

5. Vous arrive-t-il de voir des choses que les autres ne peuvent pas voir ou semblent ne pas voir ? 15 %


100
75
50
25
0
96
81
98
96
91
SIPS - Symptômes Négatifs
Fréquence
6.0
5.0
4.0
3.0
2.0
1.0
0
2.0
2.0
3.0
4.0
3.0
SIPS - Symptômes négatifs
Sévérité
SEVERITY SCALE
0 Absent
1 Questionably present
2 Mild
3 Moderate
4 Moderately Severe
5 Severe but not psychotic
6 Severe and Psychotic
Social Anhedonia / Withdrawal
Avolition
Expression of Emotion
Ideational Richness
Occupational Functioning

Symptômes négatifs et adaptation



Réflexions sur le traitement des symptômes psychotiques

- Neuroleptiques (Risperdal éventuellement en association avec le Solian)
- Traiter les symptômes anxieux et dépressifs associés
- Traitements 22q11 spécifiques
- Omega 3-6

CME

Catecholamines in patients with 22q11.2 deletion syndrome and the low-activity COMT polymorphism

W.D. Graf, MD; A.S. Unis, MD; C.M. Yates, PhD; S. Sulzbacher, PhD; M.B. Dinulos, MD; R.M. Jack, PhD; K.A. Dugaw, MS; M.N. Paddock, BS; and W.W. Parson, PhD

Article abstract—*Objective:* To investigate catecholamine phenotypes and the effects of a tyrosine hydroxylase inhibitor in individuals with the 22q11.2 deletion syndrome and low-activity catechol-*O*-methyltransferase (COMT). *Background:* Many persons with the 22q11.2 deletion syndrome suffer severe disability from a characteristic ultrarapid-cycling bipolar disorder and associated "affective storms." One etiologic hypothesis for this condition is that deletion of the *COMT* gene from one chromosome 22 results in increased catecholamine neurotransmission, particularly if the undeleted chromosome 22 encodes a variant of COMT with low activity. *Methods:* In a preliminary study, plasma, urine, and CSF catecholamines and catecholamine metabolites were measured in four teenage patients with a neuropsychiatric condition associated with 22q11.2 deletion and the low-activity COMT polymorphism on the nondeleted chromosome. In these four patients, and an additional institutionalized adult with the condition, an uncontrolled, open-label trial of metyrosine was administered in an attempt to lower catecholamine production and to alleviate symptoms. *Results:* Mild elevations of baseline CSF homovanillic acid (HVA) were found in three of four patients and a moderate reduction in CSF HVA after metyrosine treatment in the patient with the highest pretreatment concentration. The course of the five patients during the clinical trial is described. *Conclusions:* In patients with the 22q11.2 deletion syndrome and low-activity COMT, controlled studies of pharmacologic agents that decrease catecholamine production, block presynaptic catecholamine storage, or enhance *S*-adenosylmethionine, the cosubstrate of COMT, are warranted.

NEUROLOGY 2001;57:410–416

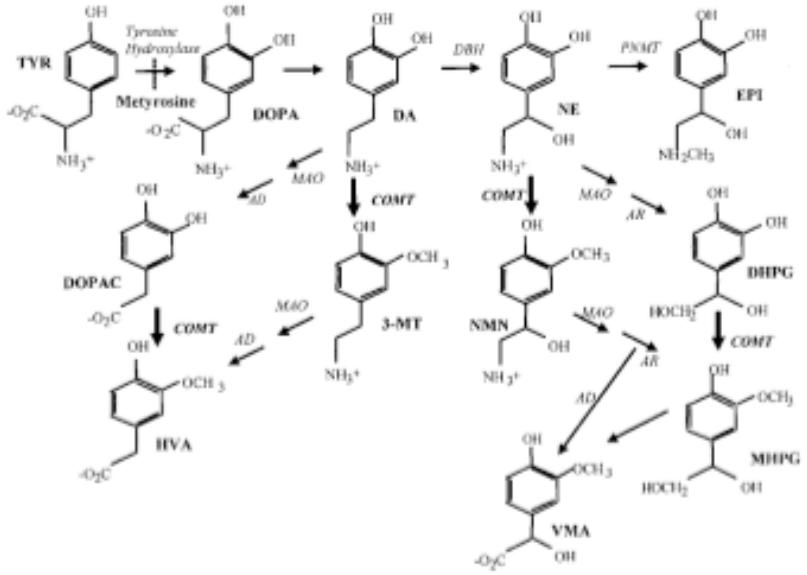


Figure 1. Pathways of catecholamine metabolism. AD = aldehyde dehydrogenase; AR = aldehyde reductase; COMT = catechol-O-methyltransferase; DHPG = 3,4-dihydroxyphenylglycol; DA = dopamine; DBH = dopamine-β-hydroxylase; DOPA = dihydroxyphenylacetic acid; DOPAC = 3,4-dihydroxyphenylacetic acid; EPI = epinephrine; NE = norepinephrine; 3-MT = 3-methoxytyramine; NMN = normetanephrine; MAO = monoamine oxidase; MHPG = 3-methoxy-4-hydroxyphenylglycol; PNMT = phenylethanolamine-N-methyltransferase; VMA = vanillylmandelic acid. Reactions catalyzed by COMT are indicated with bold arrows. Conversion of EPI to metanephrine (not shown) also requires COMT and is analogous to the conversion of NE to NMN.

Replacement of antipsychotic and antiepileptic medication by L-α-methyldopa in a woman with velocardiofacial syndrome

James F. O'Hanlon[a], Rand C. Ritchie[b], Edward A. Smith[c] and Rashiklal Patel[d]

We report the case of a 23-year-old woman with velocardiofacial syndrome (VCFS) and a history of psychosis and seizures. She had been treated with conventional antipsychotic and antiepileptic drugs for 10 and 3 years, respectively. However, she continued to experience occasional hallucinations and paroxysmal jerking of the extremities. L-α-methyldopa 500 mg b.i.d. (later reduced to 250 mg t.i.d.) was added to her regimen. Hallucinations and seizures stopped shortly. Over the course of approximately 1 year, the previous medications were discontinued without recurrence of psychotic and epileptic symptoms. Eventually, improved mental functions and behaviour enabled her transition from living in a licensed residential facility to sharing a private residence with a partner. VCFS is associated with haploinsufficiency of catecholamine-*O*-methyltransferase, leading to excessive extraneuronal catecholamine concentrations. α-Methyldopa inhibits catecholamine neurotransmission in a variety of ways. It is possible that the drug compensated for genetically disturbed catecholamine transmission thus achieving beneficial effects in this case. *Int Clin Psychopharmacol* 18:117–119

International Clinical Psychopharmacology 2003, 18:117–119

Keywords: alpha-methyldopa, case study, catecholamine-*O*-methyltransferase, dopamine, mania, noradrenaline, norepinephrine, psychosis, velocardiofacial syndrome

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Long-Chain ω-3 Fatty Acids for Indicated Prevention of Psychotic Disorders

A Randomized, Placebo-Controlled Trial

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Context: The use of antipsychotic medication for the prevention of psychotic disorders is controversial. Long-chain ω-3 (omega-3) polyunsaturated fatty acids (PUFAs) may be beneficial in a range of psychiatric conditions, including schizophrenia. Given that ω-3 PUFAs are generally beneficial to health and without clinically relevant adverse effects, their preventive use in psychosis merits investigation.

Objective: To determine whether ω-3 PUFAs reduce the rate of progression to first-episode psychotic disorder in adolescents and young adults aged 13 to 25 years with subthreshold psychosis.

Design: Randomized, double-blind, placebo-controlled trial conducted between 2004 and 2007.

Setting: Psychosis detection unit of a large public hospital in Vienna, Austria.

Participants: Eighty-one individuals at ultra-high risk of psychotic disorder.

Interventions: A 12-week intervention period of 1.2-g/d ω-3 PUFA or placebo was followed by a 40-week monitoring period; the total study period was 12 months.

Main Outcome Measures: The primary outcome measure was transition to psychotic disorder. Secondary outcomes included symptomatic and functional changes. The ratio of ω-6 to ω-3 fatty acids in erythrocytes was used to index pretreatment vs posttreatment fatty acid composition.

Results: Seventy-six of 81 participants (93.8%) completed the intervention. By study's end (12 months), 2 of 41 individuals (4.9%) in the ω-3 group and 11 of 40 (27.5%) in the placebo group had transitioned to psychotic disorder ($P=.007$). The difference between the groups in the cumulative risk of progression to full-threshold psychosis was 22.6% (95% confidence interval, 4.8-40.4). ω-3 Polyunsaturated fatty acids also significantly reduced positive symptoms ($P=.01$), negative symptoms ($P=.02$), and general symptoms ($P=.01$) and improved functioning ($P=.002$) compared with placebo. The incidence of adverse effects did not differ between the treatment groups.

Conclusions: Long-chain ω-3 PUFAs reduce the risk of progression to psychotic disorder and may offer a safe and efficacious strategy for indicated prevention in young people with subthreshold psychotic states.

Trial Registration: clinicaltrials.gov Identifier: NCT00396643

Arch Gen Psychiatry. 2010;67(2):146-154

Conclusion

- Certains troubles sont fréquents mais n'ont qu'une implication modérée ou répondent bien au traitement
- Les symptômes psychotiques positifs sont fréquents mais généralement peu intenses
- Dans tous les cas une évaluation à intervalles réguliers du fonctionnement psychique est nécessaire pour permettre d'identifier et de traiter précocement les difficultés rencontrées

Questions

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