Psychiatric disturbances in Prader-Willi Syndrome

Felice Iasevoli

Ambulatorio per le Farmacoresistenze in Psichiatria

UOSD Psichiatria e Psicofarmacoresistenze

Responsabile: prof. Andrea de Bartolomeis

Behavioral Features in PWS

- Intellectual disability
- Language difficulties
- Autistic conducts
- Temper tantrums
- Stubborness
- Impulsivity, irritability, emotional liability
- Self-injury (mostly: skin-picking)

Behavioral and psychiatric disorders in Prader-Willi syndrome: A population study in Japan

Rika Hiraiwa [a,b,*], Yoshihiro Maegaki [a], Akira Oka [a,c], Kousaku Ohno [a]

Table 1
Comparison of past 5 years prevalence of behavior problems among different age groups of Prader-Willi syndrome (PWS)

Behavior problems	Age range[a] (years)	Group 1 ($n = 34$) (%)	Group 2 ($n = 57$) (%)	Group 3 ($n = 45$) (%)	Group 4 ($n = 29$) (%)
Stubbornness	2–31	50.0	82.5	77.8	82.8
Hyperphagia	2–31	14.7	52.6	53.3	82.8
Food stealing	2–31	11.8	49.1	71.1	79.3
Temper tantrums	2–31	35.3	57.9	48.9	75.9
Lying	5–31	5.9	50.9	68.9	72.4
Emotional lability	2–31	14.7	35.1	31.1	65.5
Self-injurious behavior (skin picking)	2–31	35.3	56.1	62.2	58.6
Aggressive behavior	4–31	5.9	31.6	37.8	58.6
Repetitive speech	3–31	52.9	64.9	60.0	55.2
Hypersomnia	4–31	2.9	21.1	20.0	51.7
Laziness	6–31	0.0	12.3	4.4	34.5
Stealing	6–31	0.0	12.3	28.9	24.1
Compulsive behavior	6–27	0.0	19.3	11.1	20.7
Passage related behavior disorder	5–27	2.9	22.8	20.0	20.7
Wandering	5–31	2.9	19.3	8.9	17.2
Pica	2–25	2.9	7.0	2.2	10.3
Sexual behavior disorder	12–21	0.0	0.0	6.7	10.3
Hyperactivity	2–27	2.9	14.0	2.2	6.9
One or more of the problems	2–31	79.4	96.5	100.0	96.6

Note. Group 1, 2–5 years; group 2, 6–11 years; group 3, 12–17 years; group 4, 18–31 years.
[a] Age range of the persons with PWS at the time of the survey, who had showed the behavior problem in th

Brain & Development 29 (2007) 535–542

Table 4
Comparison of past 5 years prevalence of behavior problems between young adults with Prader-Willi syndrome (PWS) and persons with intellectual disability (ID) of other etiologies

Behavior problems	PWS ($n = 29$) (%)	ID ($n = 42$) (%)
Stubbornness	82.8***	23.8
Hyperphagia	82.8***	4.8
Temper tantrums	75.9***	16.7
Self-injurious behavior (skin picking)	58.6***	4.8
Hypersomnia	51.7***	0.0
Laziness	34.5***	0.0
Stealing	24.1**	0.0
Compulsive behavior	20.7	9.5
Passage related behavior disorder	20.7	7.1
Wandering	17.2**	0.0
Pica	10.3	0.0
Sexual behavior disorder	10.3	2.4
Hyperactivity	6.9	16.7

** $p < 0.01$.
*** $p < 0.001$.

Table 2
Comparison of past 5 years prevalence of psychiatric symptoms among different age groups of Prader-Willi syndrome (PWS)

Psychiatric symptoms	Age range[a] (years)	Group 1 ($n = 34$) (%)	Group 2 ($n = 57$) (%)	Group 3 ($n = 45$) (%)	Group 4 ($n = 29$) (%)
Inactivity, lack of spirit	10–31	0.0	3.5	6.7	20.7
Depressive state	10–31	0.0	1.8	2.2	10.3
Manic state	10–21	0.0	1.8	2.2	6.9
Hallucination	5–22	2.9	1.8	2.2	10.3
Delusion	14–31	0.0	0.0	4.4	20.7
One or more of the symptoms	5–31	2.9	3.5	13.3	37.9

Note. Group 1, 2–5 years; group 2, 6–11 years; group 3, 12–17 years; group 4, 18–31 years.
[a] Age range of the persons with PWS at the time of the survey, who had showed the psychiatric symptom in the past five years.

Table 5
Comparison of past 5 years prevalence of psychiatric symptoms between young adults with Prader-Willi syndrome (PWS) and persons with intellectual disability (ID) of other etiologies

Psychiatric symptoms	PWS ($n = 29$) (%)	ID ($n = 42$) (%)
Inactivity, lack of spirit	20.7**	0.0
Delusion	20.7**	0.0
Depressive state	10.3	7.1
Hallucination	10.3	2.4
Manic state	6.9	4.8
One or more of the symptoms	37.9*	11.9

* $p < 0.05$.
** $p < 0.01$.

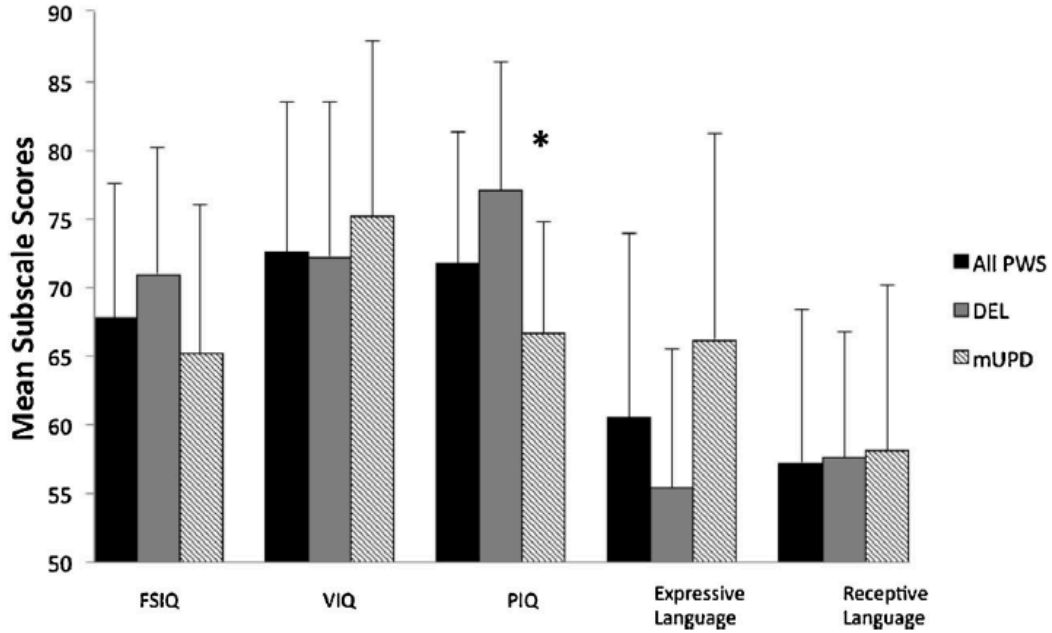

Fig. 1. Mean IQ and CELF-IV Language Domain scores by group. FSIQ: Full Scale Intelligence Quotient; VIQ: verbal IQ; PIQ: performance IQ. *$p < .05$, DEL > mUPD. *Within group comparisons.* For the mUPD group: VIQ > PIQ ($p < .01$), Expressive Language > Receptive Language ($p < .05$). For the total sample, mUPD, and DEL groups: VIQ > Expressive Language ($p < .01$), VIQ vs. Receptive Language ($p < .01$).

Table 2
CELF-IV domain and subtest scores by group.

	PWS-All ($n = 35$)	DEL ($n = 10$)	mUPD ($n = 14$)	*F*-Value
Core Language Score	60.37 (13.8)	54.90 (11.2)	64.64 (14.3)	2.804
Word Classes – Total	3.17 (2.3)	3.10 (2.1)	3.14 (2.6)	.009
Word Definitions[a]	5.10 (2.9)	4.33 (3.0)	5.44 (2.5)	.689
Receptive Language	57.19 (11.1)	57.56 (9.1)	58.07 (12.0)	.023
Word Classes – Receptive	3.11 (2.6)	3.00 (2.1)	2.86 (2.7)	.096
Semantic Relationships[b]	2.48 (2.4)	2.29 (1.7)	2.29 (2.2)	.041
Understanding Spoken Paragraphs[a]	2.58 (2.0)	2.75 (1.8)	3.11 (2.7)	.120
Expressive Language	60.54 (13.3)	55.40 (10.0)	66.14 (14.9)	3.324
Recalling Sentences[*]	3.09 (2.8)	1.5 (.97)	4.79 (3.0)	10.04
Formulated Sentences	3.94 (3.1)	3.40 (2.8)	4.71 (3.5)	.661
Word Classes – Expressive	3.77 (2.4)	3.70 (2.3)	3.93 (2.7)	.051
Sentence Assembly[c]	2.48 (2.6)	2.57 (2.8)	1.29 (.8)	1.008

Autism Spectrum Disorder in Prader–Willi Syndrome: A Systematic Review

Jeffrey A. Bennett,[1,2]* Tamara Germani,[1,2] Andrea M. Haqq,[2] and Lonnie Zwaigenbaum[1,2]

Am J Med Genet Part A 167A:2936–2944.

TABLE II. ASD in PWS Prevalence

First author, year of publication	N (% male)	# DEL	# UPD	ASD symptomatology assessment	Total	%	DEL	%	UPD	%
Ali [2014]	15 (53)	10	5	Childhood autism rating scale	4	26.7	0	0	4	80
Akefeldt [1999]	44 (64)	–	–	Clinical diagnosis	1	2.27	–	–	–	–
Beardsmore [1998]	23 (39)	–	–	PAS-ADD	0	0	–	–	–	–
Descheemaeker [2002]	53 (57)	–	–	Clinical diagnosis	4	7.55	–	–	–	–
Descheemaeker [2006]	59 (53)	40	19	PDD-MR scale	11	18.6	6	15	5	26.3
Dimitropoulos [2013]	39 (36)	20	19	SRS, social competency inventory	22	56.4	7	35	15	78.9
Flores [2011]	45 (44)	24	20	Repetitive behaviour scale-revised; SCQ	12	26.7	5	20.8	7	35
Hou [1998]	66 (68)	48	18	ADI	10	15.2	6	12.5	4	22.2
Lo [2013]	66 (55)	25	41	Dutch ToM Test-R, DISCO	24	36.4	7	28	14	34.1
Moss [2009]	189 (53)	–	–	ASQ, repetitive behavior questionnaire	77	40.7	–	–	–	–
Reilly [2014][a,b]	110 (54)	56	36	Parent report about clinical diagnosis	14	12.7	7	12.5	4	11.1
Veltman [2004]	63 (nr)	31	32	ASQ	23	36.5	9	29	14	43.8
Zyga [2014]	14 (57)	–	–	SRS, ADOS	8	57.1	–	–	–	–
Totals	786	254	190	–	210	26.7	47	18.5	67	35.3

nr, not reported.
[a]Data for genetic subtype obtained from correspondence with authors.
[b]Genetic subtype not known for every individual.

Social Responsiveness and Competence in Prader-Willi Syndrome: Direct Comparison to Autism Spectrum Disorder

Table 2 Social responsiveness and competence scores by participant group

	PWS-DEL (n = 20)	PWS-mUPD (n = 19)	ASD (n = 19)	F value, pairwise comparison
SRS overall score	70.60 (14.2)	82.32 (10.8)	79.79 (8.9)	7.28**, DEL < ASD & mUPD
Social awareness	63.85 (12.2)	69.53 (13.8)	67.89 (10.9)	2.34
Social cognition	69.9 (15.2)	80.42 (11.45)	77.79 (9.8)	4.19*, DEL < ASD & mUPD
Social communication	67.70 (13.9)	79.84 (11.1)	77.47 (8.9)	6.40**, DEL < ASD & mUPD
Social motivation	60.10 (11.9)	71.63 (12.2)	70.26 (10.9)	5.82**, DEL < ASD & mUPD
Autistic mannerisms	76.75 (13.8)	85.47 (11.4)	82.05 (8.3)	4.56* DEL < ASD & mUPD
SCI prosocial	3.43 (.61)	2.89 (.59)	2.54 (.55)	7.20**, ASD < DEL
SCI social initiative	3.05 (.82)	2.64 (.72)	2.51 (.73)	2.03

Values are presented as mean (SD). * $p < .05$, ** $p < .01$

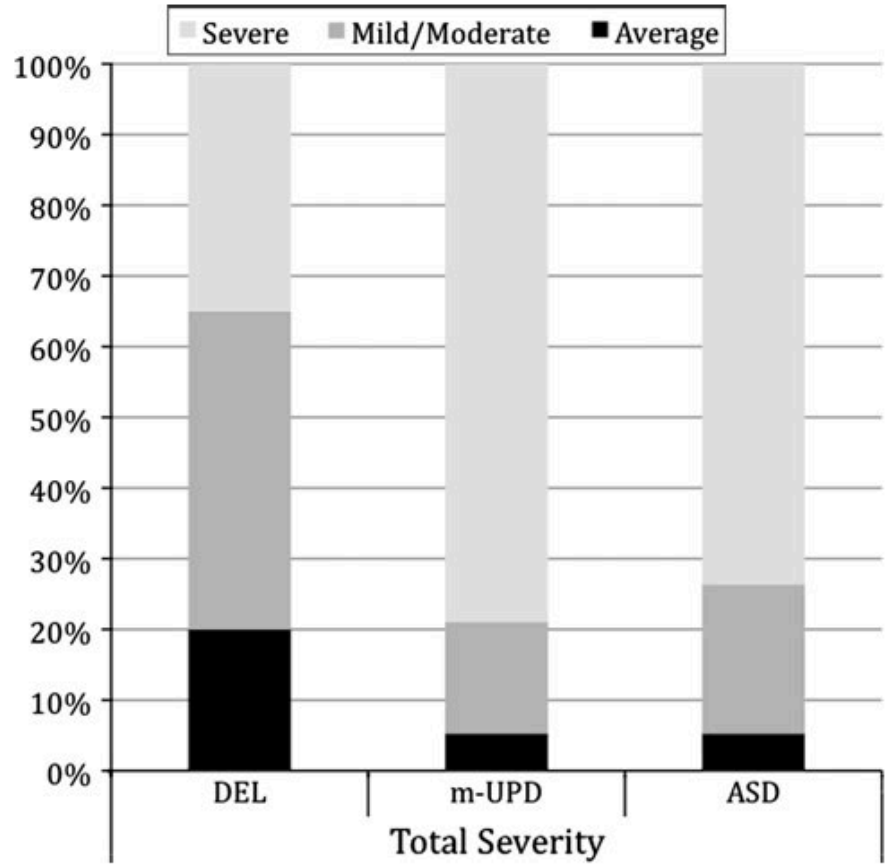

Fig. 1 The percent of participants within each group scoring in the average, mild/moderate, and severe range of social functioning

European Psychiatry 44 (2017) 47–52

Psychiatric disorders in a cohort of individuals with Prader–Willi syndrome

L. Shriki-Tal [a,b], H. Avrahamy [a], Y. Pollak [a,c], V. Gross-Tsur [a,c], L. Genstil [a], H.J. Hirsch [a], F. Benarroch [a,d,*]

Table 2
Prevalence of current DSM-IV-TR psychiatric disorders (%) and distribution of age, gender, genetic subtype and place of living of each diagnosis.

	N° of patients	Prevalence (%)	Mean age	M/F (%)	UPD (%)	DEL (%)	IC (%)	Residential facility/home (%)
Total	53		23.6	60/40	47	50	3	64/36
Odd	27	51	23.8	48/52	48	52	0	62/38
Conduct disorder	9	17	26.4	88/12	22	78	0	78/22
OCD	24	45	25.4	62/38	45	55	0	75/25
Skin picking	19	35	24.5	36/64	27	68	5	68/32
Trichotillomania	5	9	29.8	20/80	60	40	0	100/0
Depression	11	20	27.9	63/37	45	45	10	95/5
Atypicaldepression	7	63	27.6	42/58	57	28	15	85/15
Melancholic depression	4	37	28.3	100/0	25	75%	0	100/0
Schizophrenia	6	11	28.1	100/0	67	33	0	100/0
GAD	7	13	24.1	85/15	85	15	0	85/15
PTSD	4	7	32	50/50	50	25	25	100/0
Specific phobia	3	5	31.8	0/100	67	0	33	100/0
Panic disorder	1	1.8	31.6	0/100	100	0	0	100/0
Somatization disorder	5	9	31.5	20/80	20	60	20	100/0
Enuresis	9	17	22	88/12	44	56	0	78/22
Encopresis	3	5	24.6	100/0	33	67	0	67/33
ADHD	8	15	19.8	50/50	62	38	0	38/62

ODD: oppositional defiant disorder; OCD: obsessive-compulsive disorder; GAD: generalized anxiety disorder; PTSD: posttraumatic stress disorder; ADHD: attention-deficit/hyperactivity disorder.

Prader-Willi Syndrome Genetic Subtypes and Clinical Neuropsychiatric Diagnoses in Residential Care Adults

Ann M. Manzardo[1+]; Nicolette Weisensel[2,3+]; Sheryl Ayala[3]; Waheeda Hossain[1]; Merlin G. Butler[1]

Table II: Summary of Neuropsychiatric Diagnoses for PWHO Participants with Prader-Willi Syndrome

Primary Psychiatric Diagnoses	Total (N=70)	Males (N=33)	Females (N=37)	Odds# Male	95% CI	p-value
Any Psychotic Features	16 (23%)	7 (21%)	9 (24%)	0.8	0.27,2.6	0.76
Bipolar Disorder (Nonpsychotic)	15 (21%)	8 (24%)	7 (18%)	1.4	0.44,4.3	0.59
Anxiety Disorder	27 (38%)	14 (42%)	13 (35%)	1.4	0.52,3.6	0.53
Major Depressive Disorder	17 (24%)	5 (15%)	12 (32%)	0.4	0.11,1.2	0.09
Intermittent Explosive Disorder	21 (30%)	15 (45%)	6 (16%)	4.3	1.4,13.1	**0.008***
Excoriation (skin picking) Disorder	23 (33%)	8 (24%)	15 (41%)	0.5	0.17,1.3	0.15

Odds ratio for males relative to females using Logit. *p<0.05 considered significant
Additional diagnoses included: attention deficit hyperactivity disorder, conduct disorder and tic disorders. CI = confidence interval

OPEN ACCESS Freely available online

PLOS ONE

Psychiatric Illness and Intellectual Disability in the Prader–Willi Syndrome with Different Molecular Defects - A Meta Analysis

Lin Yang[1☯], Guo-dong Zhan[1☯], Jun-jie Ding[1], Hui-jun Wang[1], Duan Ma[2], Guo-ying Huang[1], Wen-hao Zhou[1*]

Study or Subgroup	Deletion Mean	SD	Total	UPD Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Boer 2002	67	12.39	9	62.4	9.86	5	3.4%	4.60 [-7.24, 16.44]
Descheemaeker 2006	57.2	16.21	40	58.4	15.56	18	6.1%	-1.20 [-9.97, 7.57]
Dykens 1999	62.97	8.83	23	70.93	11.15	23	13.9%	-7.96 [-13.77, -2.15]
Dykens 2008	62.07	12.3	55	64.96	13.07	33	15.5%	-2.89 [-8.41, 2.63]
Fox 2001	62.7	9.8	24	63.9	6.4	19	19.9%	-1.20 [-6.06, 3.66]
Milner 2005	70.78	16.21	45	69.49	16.89	47	10.3%	1.29 [-5.47, 8.05]
Roof 2000	61	9.2	24	64.1	7.9	14	15.3%	-3.10 [-8.64, 2.44]
Soni 2008	64.5	8.5	24	68.7	11.2	22	14.1%	-4.20 [-9.99, 1.59]
Zarcone 2007	62.3	55.1	41	65.2	12.1	30	1.6%	-2.90 [-20.31, 14.51]
Total (95% CI)			**285**			**211**	**100.0%**	**-2.69 [-4.86, -0.52]**

Heterogeneity: Chi² = 6.70, df = 8 (P = 0.57); I² = 0%

Test for overall effect: Z = 2.43 (P = 0.02)

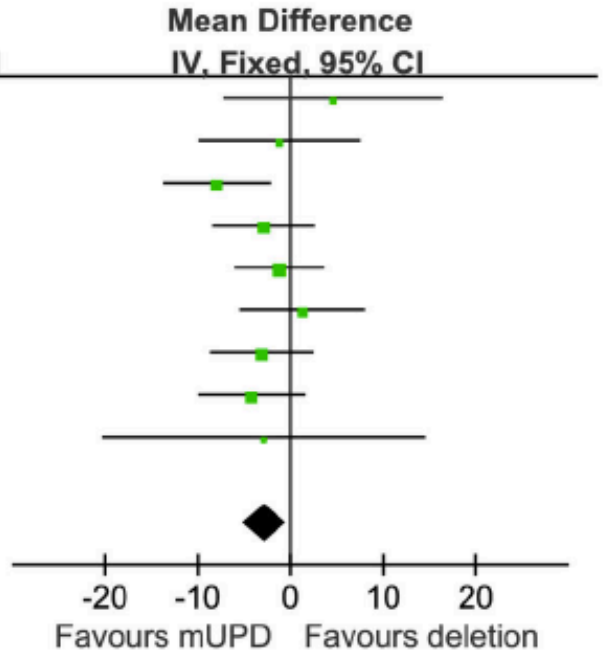

Figure 3. Meta analysis of the FSIQ in DEL and UPD groups.

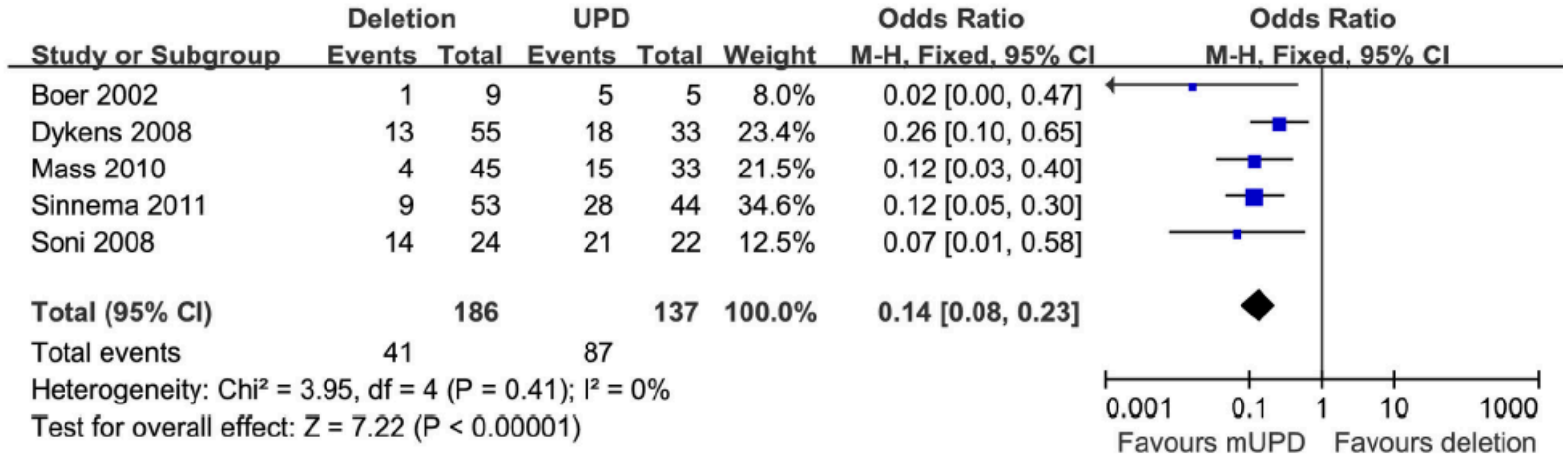

Figure 7. Metaanalysis of the prevalence of psychosis in DEL and UPD groups.

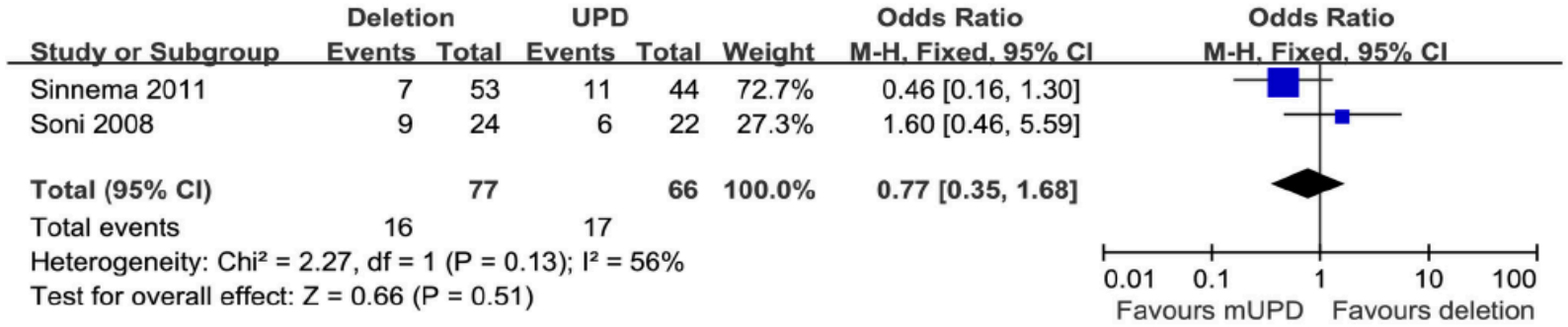

Figure 8. Metaanalysis of the prevalence of depression in DEL and UPD groups.

i: 10.1371/journal.pone.0072640.g008

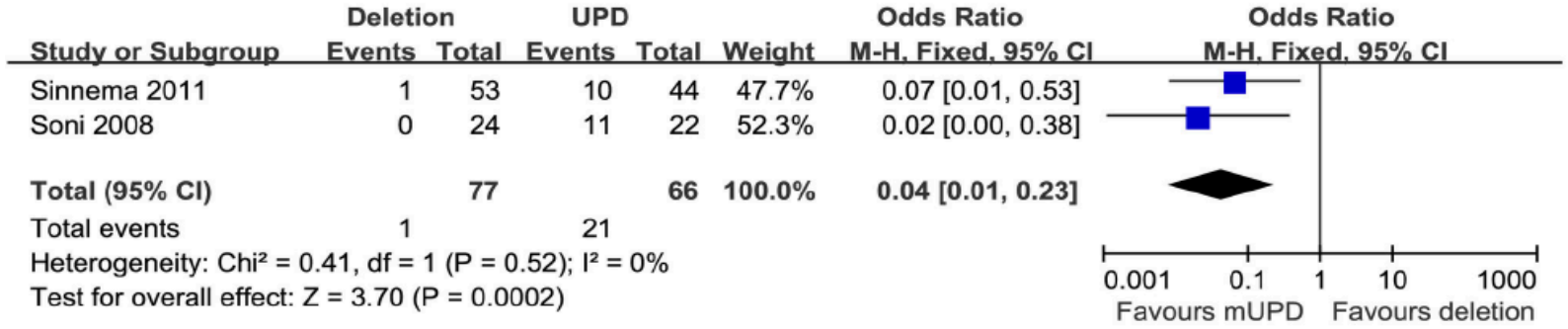

Figure 9. Metaanalysis of the prevalence of bipolar in DEL and UPD groups.

Possible Therapeutic Approaches

- Antipsychotics
  - Only limited studies with risperidone
  - Risk of weight increase
- SSRI
  - No obvious improvement of OCD, mood disorders, or food intake
  - Risk of increased outbursts
- Topiramate
  - Reports of good efficacy on temper tantrums and food intake
  - Risk of inducing psychotic symptoms and irritability
- N-acetyl-cysteine
  - Found to be effective against skin-picking
- Mood stabilizers
  - No studies at the moment