

Table S1. Changes to the original protocol.

STEPS	DATE
REB approval	2014/07/18
Minor changes to protocol: <ul style="list-style-type: none"> - Dr Fabienne CYPRIEN is not an investigator of this study anymore. - Add Dr Aurélie CHOPIN as an investigator. - Clarification in the protocol that the self-rated Beck SSI is fulfilled in addition to the clinician-rated Beck SSI. - Stop using QIDS-SR16 as it is redundant for the assessment of depression with the IDS-30 and increase the duration of patient's assessment 	2015/07/01
Minor changes to protocol: <ul style="list-style-type: none"> - Add Dr Fabrice JOLLANT as an investigator - Modify the professional location for Prof. Franck BELLIVIER - Modify the way the biobank is constituted to improve the quality of samples: <ul style="list-style-type: none"> + modify the order of blood samples + modify the tubes used for samples + Modify the location of sample storage 	2015/11/04
Minor changes to protocol: <ul style="list-style-type: none"> - Increase the duration of recruitment by 18 months to reach the targeted sample size 	2016/04/13
Minor changes to protocol: <ul style="list-style-type: none"> - Increase the duration of recruitment by 12 months to reach the targeted sample size - Add CMME in Paris as a recruitment center - Several questionnaires are stopped at endpoints 40min, 120min or 4h to reduce the burden of these assessments 	2017/09/13
Minor changes to protocol: <ul style="list-style-type: none"> - Increase the duration of recruitment by 6 months to reach the targeted sample size 	2018/07/04

Table S2. Sample size calculation

For each diagnostic category, 26 subjects per arm would make it possible to demonstrate an absolute difference of approximately 45% in the rate of resolution of suicidal ideation at 72 hours (15% in the placebo arm versus approximately 60% in the Ketamine arm), with a power of 85% and an overall two-sided alpha risk of 5% (Bonferoni's correction was applied for the performance of 3 ($\alpha=0.017$) or 4 ($\alpha=0.013$) tests. So the total number of subjects to include is 156. The calculation was carried out with nQuery software version 8.7.2.0

Compute Proportion for Two-Sample Chi-Squared Test



Columns 1-5	1	2	3	4	5
Test Significance Level, α	0.013	0.017			
1 or 2 Sided Test?	2	2	2	2	2
Smaller Proportion, π_1	0.150	0.150			
Larger Proportion, π_2	0.609	0.594			
Power (%)	85	85			
Sample Size per Group, n	26	26			

Table S3: Baseline characteristics of the bipolar disorder group

	Placebo (n=26)	Ketamine (n=26)
Sex		
Male	8 (30.8%)	6 (23.1%)
Female	18 (69.2%)	20 (76.9%)
Age (years)	46 [18-71]	39.5 [22-75]
Height (cm)	166.5 (160-172)	166 (164-170)
BMI (kg/m ²)	25.7 (22.6 - 27.5)	23.1 (21.2 - 27.9)
SSI suicidal ideas score, clinician-rated	20 (18 - 24)	20.5 (16.0 - 26.5)
SSI suicidal ideas score, patient-rated	17.5 (14.8 - 19.0)	16.5 (12.0 - 18.0)
CSSRS suicidal ideation intensity score	22.0 [18.5 - 24.0]	20.0 [16.3 - 23.0]
MINI - Severe suicidal ideas	24 (92.3%)	25 (96.2%)
PPP-VAS physical pain score	2.1 (0.0 - 4.9)	2.0 (0.0 - 5.0)
PPP-VAS psychological pain score	8.1 (6.8 - 8.8)	6.8 (6.0 - 8.4)
BHS hopelessness score	15.0 (13.0 - 16.3)	15 (12 - 17)
IDS-C30 depression score	39 (35 - 45)	39.0 (31.8 - 48)
Major depressive episode - current	16 (61.5%)	15 (57.7%)
Dysthymia - current	0 (0%)	1 (3.8%)
Manic episodes - past	17 (65.4%)	14 (53.8%)
Hypomanic episodes - past	10 (38.5%)	11 (42.3%)
Panic disorder - current	1 (3.8%)	6 (23.1%)
Agoraphobia - current	4 (15.4%)	5 (19.2%)
Social phobia - current	4 (15.4%)	6 (23.1%)
Generalized anxiety - current	3 (11.5%)	3 (11.5%)
Obsessive-compulsive disorder - current	0 (0%)	1 (3.8%)
Post-traumatic stress disorder - current	2 (7.7%)	2 (7.7%)
Alcohol dependence - past	2 (7.7%)	3 (11.5%)
Substance dependence - past	2 (7.7%)	2 (7.7%)
Anorexia nervosa - current	0 (0%)	0 (0%)
Bulimia nervosa - current	2 (7.7%)	2 (7.7%)
Previous history of suicide attempt	26 (100%)	23 (92%)
Medication at Day 3 :		
Lithium	4 (15.4 %)	1 (3.8 %)
Antipsychotics	16 (61.5 %)	12 (46.2 %)
Antiepileptics	11 (42.3 %)	4 (15.4 %)
Antidepressants	12 (46.2 %)	8 (30.8 %)
Anxiolytics	12 (46.2 %)	14 (53.8 %)
Hypnotics	3 (11.5 %)	2 (7.7 %)
Other psychotropic medication	1 (3.8 %)	1 (3.8 %)
Antalgic	1 (3.8 %)	5 (19.2 %)
Other medication	7 (26.9 %)	9 (34.6 %)

Data are n (%), median (IQR) or median [range], mean (SD), or n/N (%). BMI=body-mass index. SSI=Beck scale for suicidal ideation. CSSRS =Columbia severity suicide rating scale. MINI: 7th version (7.0.2) of the Mini International Neuropsychiatric Interview. PPP-VAS=Physical and psychological pain – visual analog scale. BHS: Beck hopelessness scale. IDS=30-item inventory for depressive symptomatology, clinician-rated version.

Table S4: Baseline characteristics of the depressive disorder group

	Placebo (n=30)	Ketamine (n=26)
Sex		
Male	17 (56.7%)	7 (26.9%)
Female	13 (43.3%)	19 (73.1%)
Age (years)	40.5 [18 - 76]	40 [19 - 67]
Height (cm)	170.0 (163.3 – 177.0)	165.0 (160.0 – 170.8)
BMI (kg/m ²)	22.2 (19.7 - 24.9)	23.5 (20.0 - 29.1)
SSI suicidal ideas score, clinician-rated	16.5 (13.3 - 22.0)	23.0 (19.5 - 27.5)
SSI suicidal ideas score, patient-rated	15 (12 - 19)	17.0 (15.5 - 21.3)
CSSRS suicidal ideation intensity score	18 [12 - 24]	20 [11 - 25]
MINI - Severe suicidal ideas	23 (79.3%)	26 (100%)
PPP-VAS physical pain score	1.90 (0.03 - 5.00)	2.55 (0.00 - 6.85)
PPP-VAS psychological pain score	7.1 (6.0 - 8.2)	8.0 (6.4 - 9.0)
BHS hopelessness score	14.0 (11.5 - 17.5)	17 (14 - 18)
IDS-C30 depression score	37.5 (33.3 - 48.0)	46.5 (37.0 - 51.0)
Major depressive episode - current	22 (73.3%)	17 (65.4%)
Dysthymia - current	3 (10%)	4 (15.4%)
Manic episodes - past	0 (0%)	0 (0%)
Hypomanic episodes - past	0 (0%)	0 (0%)
Panic disorder - current	5 (17.2%)	4 (15.4%)
Agoraphobia - current	6 (20.7%)	2 (7.7%)
Social phobia - current	8 (27.6%)	4 (15.4%)
Generalized anxiety - current	9 (30%)	8 (30.8%)
Obsessive-compulsive disorder - current	1 (3.4%)	2 (7.7%)
Post-traumatic stress disorder - current	5 (16.7%)	5 (19.2%)
Alcohol dependence - past	4 (13.3%)	2 (7.7%)
Substance dependence - past	4 (13.3%)	2 (7.7%)
Anorexia nervosa - current	0 (0%)	0 (0%)
Bulimia nervosa - current	1 (3.3%)	2 (7.7%)
Previous history of suicide attempt	20 (69.0%)	24 (92.3%)
Medication at Day 3 :		
Lithium	0 (0 %)	1 (3.8 %)
Antipsychotics	13 (43.3 %)	8 (30.8 %)
Antiepileptics	0 (0 %)	0 (0 %)
Antidepressants	12 (40 %)	5 (19.2 %)
Anxiolytics	18 (60 %)	14 (53.8 %)
Hypnotics	3 (10 %)	1 (3.8 %)
Other psychotropic medication	2 (6.7 %)	3 (11.5 %)
Antalgic	0 (0 %)	2 (7.7 %)
Other medication	10 (33.3 %)	9 (34.6 %)

Data are n (%), median (IQR) or median [range], mean (SD), or n/N (%). BMI=body-mass index. SSI=Beck scale for suicidal ideation. CSSRS =Columbia severity suicide rating scale. MINI: 7th version (7.0.2) of the Mini International Neuropsychiatric Interview. PPP-VAS=Physical and psychological pain – visual analog scale. BHS: Beck hopelessness scale. IDS=30-item inventory for depressive symptomatology, clinician-rated version.

Table S5: Baseline characteristics of the other diagnoses group

	Placebo (n=27)	Ketamine (n=21)
Sex		
Male	6 (22.2%)	6 (28.6%)
Female	21 (77.8%)	15 (71.4%)
Age (years)	38.0 [22.0 - 50.5]	30 [26 - 46]
Height (cm)	163.0 (159.0 - 170.5)	165 (158 - 170)
BMI (kg/m ²)	26.2 (21.3 - 30.4)	27.6 (21.8 - 34.0)
SSI suicidal ideas score, clinician-rated	23.0 (16.5 - 26.5)	20 (16 - 26)
SSI suicidal ideas score, patient-rated	19.0 (14.3 - 23.0)	16.5 (14.0 - 19.3)
CSSRS suicidal ideation intensity score	18 [12 - 24]	20 [13 - 25]
MINI - Severe suicidal ideas	24 (88.9%)	20 (95.2%)
PPP-VAS physical pain score	1.6 (0.0 - 4.0)	1.5 (0.0 - 4.5)
PPP-VAS psychological pain score	9.1 (7.9 - 10.0)	8 (7 - 9)
BHS hopelessness score	16.0 (11.5 - 17.0)	16.0 (13.8 - 17.0)
IDS-C30 depression score	33 (28 - 40)	31 (23 - 37)
Major depressive episode - current	0 (0%)	0 (0%)
Dysthymia - current	2 (7.4%)	3 (14.3%)
Manic episodes - past	0 (0%)	0 (0%)
Hypomanic episodes - past	0 (0%)	0 (0%)
Panic disorder - current	2 (7.4%)	1 (4.8%)
Agoraphobia - current	2 (7.4%)	4 (19.0%)
Social phobia - current	5 (18.5%)	3 (14.3%)
Generalized anxiety - current	4 (14.8%)	3 (14.3%)
Obsessive-compulsive disorder - current	0 (0%)	0 (0%)
Post-traumatic stress disorder - current	4 (14.8%)	5 (23.8%)
Alcohol dependence - past	0 (0%)	1 (4.8%)
Substance dependence - past	0 (0%)	0 (0%)
Anorexia nervosa - current	1 (3.7%)	0 (0%)
Bulimia nervosa - current	2 (7.4%)	2 (9.5%)
Previous history of suicide attempt	24 (88.9%)	20 (95.2%)
Medication at Day 3 :		
Lithium	0 (0 %)	0 (0 %)
Antipsychotics	7 (25.9 %)	10 (47.6 %)
Antiepileptics	1 (3.7 %)	1 (4.8 %)
Antidepressants	4 (14.8 %)	5 (23.8 %)
Anxiolytics	12 (44.4 %)	10 (47.6 %)
Hypnotics	4 (14.8 %)	2 (9.5 %)
Other psychotropic medication	0 (0 %)	1 (4.8 %)
Antalgic	1 (3.7 %)	3 (14.3 %)
Other medication	9 (33.3 %)	5 (23.8 %)

Data are n (%), median (IQR) or median [range], mean (SD), or n/N (%). BMI=body-mass index. SSI=Beck scale for suicidal ideation. CSSRS =Columbia severity suicide rating scale. MINI: 7th version (7.0.2) of the Mini International Neuropsychiatric Interview. PPP-VAS=Physical and psychological pain – visual analog scale. BHS: Beck hopelessness scale. IDS=30-item inventory for depressive symptomatology, clinician-rated version.

Table S6. Outcome of the scales used at each assessment point in each arm (P: Placebo, K: Ketamine).

	Baseline		40 min		120 min		4 hours		24 hours		48 hours		72 hours		96 hours		2 weeks		4 weeks		6 weeks	
Arm	P	K	P	K	P	K	P	K	P	K	P	K	P	K	P	K	P	K	P	K	P	K
Clinician-rated SSI: median (Q1,Q3)	20 (16, 24)	22 (16, 26)	14 (10, 21)	7 (2, 14)	16 (10, 21)	6 (1, 12)	14.0 (7.8, 21.2)	5 (1, 12.5)	11.5 (5.3, 19.1)	4.5 (0.0, 12.8)	10 (4, 18)	3 (0, 10)	8.0 (2.0, 15.5)	1 (0, 8)	7 (1, 16)	1 (0, 6)	7 (1, 16)	1.0 (0.0, 9.5)	4.5 (0.0, 13.8)	1.0 (0.0, 7.5)	1 (0, 11)	0.0 (0.0, 7.8)
Clinician-rated SSI, score below 3: n (%)	0	0	5 (6.3)	28 (38.4)	7 (8.6)	31 (42.5)	6 (7.3)	32 (43.8)	14 (17.1)	33 (45.2)	19 (23.5)	38 (52.8)	25 (31.6)	46 (63.0)	25 (33.8)	50 (72.5)	28 (39.4)	39 (59.1)	33 (48.5)	40 (66.7)	36 (56.3)	41 (69.5)
Self-rated SSI: median (Q1,Q3)	17 (14, 20)	17 (13, 20)	16 (11, 20)	12 (7, 17)	16 (11, 20)	10 (6, 16)	15 (11, 19)	10.0 (6.0, 16.8)	14.5 (9.0, 19.2)	8.5 (6, 14)	14 (6, 17)	9.0 (4.3, 15.0)	11.5 (7.0, 16.2)	7 (4, 12)	11.0 (8.0, 16.5)	7.0 (4.0, 11.5)	10.0 (6.0, 15.8)	6.0 (4.0, 13.8)	8.0 (5.0, 14.2)	6 (4, 11)	8 (6, 15)	6 (4, 11)
CSSSR – suicidal ideation: median (Q1,Q3)	5 (4, 5)	5 (5, 5)	-	-	-	-	-	-	1 (0, 3)	0 (0, 2)	1 (0, 3)	0 (0, 2)	0 (0, 3)	0 (0, 1)	1 (0, 3)	0 (0, 0)	1 (0, 3)	0 (0, 2)	1 (0, 3)	0 (0, 3)	0.5 (0.0, 2.8)	0 (0, 2)
CSSSR – suicidal ideation (yes/no): n (%)	83 (100)	73 (100)	-	-	-	-	-	-	51 (65.2)	35 (47.9)	45 (55.6)	30 (41.7)	38 (48.1)	23 (31.9)	40 (52.6)	17 (24.3)	42 (59.2)	31 (46.3)	40 (58)	26 (43.3)	33 (50)	24 (40)
CSSSR – intensity of	18.9	19.4	-	-	-	-	-	-	15.4 (3.7)	15.9	15.5 (4.0)	14.9	16.0 (3.7)	15.5	15.2 (3.2)	15.4	14.7 (3.4)	13.5	14.1	13.8	13.5	13.2

suicidal ideation: mean (SD)	(3.9)	(3.8))	(3.8))	(4.1))	(4.4))	(4.0))	(3.9)	(4.0)	(4.5)	(3.8)	(4.6)
PPP-VAS, current physical pain: median (Q1,Q3)	2 (0, 5)	1.9 (0, 5.3)	0.7 (0, 4.4)	0.2 (0, 4.3)	0.9 (0, 4.4)	0.2 (0, 2.2)	1.4 (0, 4.9)	0.1 (0, 2.6)	1.0 (0, 4.2)	0.2 (0, 3.3)	0.5 (0, 3.0)	0.1 (0, 4.0)	0.5 (0, 3.5)	0.1 (0, 3.0)	0.9 (0, 2.8)	0.1 (0, 2.6)	1.0 (0, 3.0)	0.1 (0, 2.2)	0 (0, 2)	0.0 (0, 1.8)	0.9 (0, 4.2)	0.05 (0, 2.1)
PPP-VAS, current mental pain: median (Q1,Q3)	8.0 (6.6 , 9.1)	8.0 (6.0 , 8.8)	7.0 (4.9 , 8.1)	5.0 (1.9 , 7.1)	7.0 (4.6 , 8.2)	4.8 (2.2 , 7.0)	7.0 (4.9 , 8.0)	4.7 (2.0 , 7.0)	6.8 (4.8 , 8.3)	4.6 (2.0 , 7.0)	5.7 (2.3 , 8.0)	4.1 (1.0 , 6.2)	5 (2, 8)	3.7 (0.3 , 6.3)	4.5 (2.0 , 8.0)	3.0 (0.1 , 6.0)	5.0 (2.0 , 6.9)	3.6 (0.2 , 6.5)	3.0 (1.0 , 6.4)	2 (0, 5)	2.4 (0.7 , 6.2)	1.5 (0.2 , 5.0)
BHS: median (Q1,Q3)	16 (12, 17)	16.0 (13.2, 17.0)	-	-	-	-	-	-	14 (9, 17)	12.0 (7.0, 16.2)	14 (9, 17)	9.5 (5.0, 17.0)	13 (8, 17)	9 (4, 15)	12 (6, 17)	9 (3, 15)	11 (7, 16)	10.0 (3.8, 16.0)	10.0 (4.8, 13.0)	6.5 (2.0, 14.5)	7 (4, 15)	7 (2, 16)
IDS-C30: mean (SD)	37.7 (9.01)	38.6 (11.2)	-	-	-	-	32.0 (10.8)	25.5 (13.5)	27.6 (10.2)	21.6 (12.8)	25.6 (11.2)	19.0 (12.5)	24.2 (12.7)	17.4 (12.1)	23.8 (12.2)	16.9 (12.2)	23.4 (12.5)	18.0 (12.5)	19.2 (12.3)	16.8 (11.5)	16.8 (10.5)	16.0 (11.7)
YMRS: median (Q1,Q3)	2.0 (0.0 , 3.5)	1 (0, 3)	-	-	-	-	-	-	1 (0, 2)	0.0 (0.0, 1.3)	1 (0, 2)	0 (0, 2)	0 (0, 2)	0 (0, 2)	0 (0, 2)	0 (0, 2)	-	-	-	-	-	-
BPRS: median (Q1,Q3)	38.7 (8.8)	37.6 (8.5)	-	-	-	-	-	-	33.5 (7.6)	29.6 (9.4)	32.0 (7.1)	27.6 (7.9)	29.6 (7.3)	26.8 (7.7)	30.6 (8.6)	27.1 (8.4)	-	-	-	-	-	-

CGI: mean (SD)	5.6 5 (0.8 5)	5.7 3 (0.7 1)	5. 36 (0. 98)	4. 59 (1 .3 8)	5.1 7 (1. 39)	4. 42 (1 .3 3)	5.2 2 (1.1 3)	4.3 6 (1.3 4)	5.13 (1.1 1)	4.26 (1.3 9)	4.79 (1.2 7)	4.14 (1.4 2)	4.55 (1.4 2)	3.81 (1.5 7)	4.58 (1.3 1)	3.70 (1.4 7)	4.13 (1.4 5)	3.58 (1.58)	3.64 (1.54)	3.52 (1.48)	3.39 (1.44)	3.41 (1.53)
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Footnotes: SSI=Beck scale for suicidal ideation. CSSRS =Columbia severity suicide rating scale. PPP-VAS=Physical and psychological pain – visual analog scale. BHS: Beck hopelessness scale. IDS-C30=30-item inventory for depressive symptomatology, clinician-rated version. YMRS: Young Mania Rating Scale. BPRS: Brief Psychiatric Rating Scale. CGI: Clinical Global Impression.

Scales used in the protocol to measure suicidal ideation and suicidal behaviors

Beck Scale for Suicidal Ideation (BSSI).

The BSSI is a 21-item questionnaire aimed to identify the presence and severity of suicidal ideation (Beck et al. 1979; Beck, Steer & Ranieri 1988; Beck, Brown & Steer 1997). It can be used as a clinician-rated questionnaire at the end of an interview, or self-rated by the patient. Items are score 0 to 2, and only the first 19 first are included in the calculation of the total score (0 to 38). Items are: Wish to live, Wish to die, Reasons for living / dying, Desire to make active suicide attempt, Passive suicide desire, Time dimension: Duration of suicide ideation / wish, Time dimension: Frequency of suicide, Attitude toward ideation / wish, Control over suicidal action / acting-out wish, Deterrents to active attempts (e.g. family, religion, irreversibility), Reason for contemplated attempt, Method: Specificity / planning of contemplated attempt, Method: Availability / opportunity for contemplated attempt, Sense of “capability” to carry out attempt, Expectancy / anticipation of actual attempt, Actual preparation for contemplated attempt, Suicide note, Final acts in anticipation of death (e.g. insurance, will), Description / concealment of contemplated suicide.

Beck AT, Kovacs M, Weissman A. Assessment of suicidal intention: the Scale for Suicide Ideation. *J Consult Clin Psychol* 1979; **47**:343-352.

Beck AT, Steer RA, Ranieri WF. Scale for Suicide Ideation: psychometric properties of a self-report version. *J Clin Psychol* 1988; **44**:499-505.

Beck AT, Brown GK, Steer RA. Psychometric characteristics of the Scale for Suicide Ideation with psychiatric outpatients. *Behav Res Ther* 1997; **35**:1039-1046.

Columbia suicide severity rating scale (CSSRS)

Developed by Posner et al. (2011) and translated into French, this scale prospectively measures the severity and intensity of suicidal ideation, the different types of suicidal behavior and the lethality of suicide attempts. The latest/lifetime version allows the practitioner to collect the history of suicidality and suicidal ideas throughout life and /or recent suicidal behavior. The scale encodes events via precise definitions. These definitions are adopted by the Centre for Disease Control and Prevention (CDC) and originate from the Columbia Classification Algorithm for Suicide Assessment (C-CASA). The C-SSRS scale is used to reduce costs and workload by providing a more accurate identification of patients at risk and the extent of treatment response. The scale is now commonly used for the evaluation of suicidal thoughts and behavior in the context of research and clinical practice in psychiatric and non-psychiatric areas.

Posner K, Brown GK, Stanley B et al. The Columbia-Suicide Severity Rating Scale: initial validity and internal consistency findings from three multisite studies with adolescents and adults. *Am J Psychiatry* 2011; **168**:1266-1277.