Assessing expectancy and suggestibility in a trial of escitalopram vs. psilocybin for depression

Supplementary materials

Analysis using treatment agnostic expectancy measure

The two items administered to measure expectancy, see Methods, are specific to the expectations regarding the escitalopram / psilocybin treatments, not the general expectancy regarding participating in the trial without knowing treatment allocation. Such treatment agnostic expectancy item could have read: '*At the end of this trial, how much improvement in your mental health do you think will occur if you receive either escitalopram every day for 6 weeks OR two full strong doses of psilocybin 3 weeks apart?*', combining the expectancy of both treatment arms. We approximated the response to such an item by taking the average of escitalopram and psilocybin expectancy, and will refer to this average as '*average trial expectancy*'. This expectancy measure is appropriate to use if we assume that patients did not gain knowledge of treatment allocation during the treatment period (the expectancy measure used in the main text assumes that patients did gain knowledge of treatment due to conspicuous drug effects). We repeated all major statistical analysis using this expectancy measure, and found the same qualitative conclusions as what is presented in the main text, statistical output can be found in the repository associated with this paper (https://github.com/szb37/psilodep2/).

Changes in expectancy between dosing sessions

As described in (Carhart-Harris et al., 2021), patients participated in two dosing sessions approximately three weeks apart, *expectancy* was measured the day before both dosing sessions as described in the Baseline Measures section.

Escitalopram expectancy non-significantly decreased (mean±SE pre-session1: 28.2±2.8; mean±SE pre-session2: 25.9±3.4) in the whole sample; similarly, *escitalopram expectancy* non-significantly decreased in the escitalopram group (mean±SE pre-session1: 29.7±4.1; mean±SE pre-session2: 26.9±4.8). *Psilocybin expectancy* non-significantly decreased (mean±SE pre-session1: 54±2.8; mean±SE pre-session2: 52.7±3.4) in the whole sample; however *psilocybin expectancy* slightly increased in the psilocybin group (mean±SE pre-session1: 57.1±3.9; mean±SE pre-session2: 62.1±4.6), but the change was not significant (paired t-test: t=0.244, df=52, p=0.81).

Supplementary tables

model	component	estimate	SE	df	t	p	
exp~(1|patient_id)+type	Intercept	28.16	2.8	101.62	9.92	< 0.001	***
exp~(1|patient_id)+type	type(psi)	25.82	3.5	54	7.43	< 0.001	***
exp~(1|patient_id)+type*trt	Intercept	29.71	3.99	99.03	7.45	< 0.001	***
exp~(1|patient_id)+type*trt	type(psi)	21.25	4.84	53.00	4.39	< 0.001	***
exp~(1|patient_id)+type*trt	trt(P)	-3.16	5.69	99.03	-0.56	0.580	
exp~(1|patient_id)+type*trt	type(psi):trt(P)	9.31	6.90	53.00	1.35	0.183	
sss~trt	Intercept	45.85	1.99	53	23.07	< 0.001	***
sss~trt	trt(P)	-2.53	2.79	53	-0.909	0.368	
abs~trt	Intercept	25.28	2.82	57	8.96	< 0.001	***
abs~trt	trt(P)	4.39	3.96	57	1.11	0.272	

Supplementary table 1: output of models assessing pre-treatment differences between treatment arms. Expectancy score is denoted by *exp, type* signifies expectancy type, i.e. escitalopram expectancy or psilocybin expectancy (baseline factor value: escitalopram expectancy), treatment allocation by *trt* (baseline factor value: escitalopram), absorption by *abs,* suggestibility by *sss.*

model	scale	trt	component	estimate	SE	t	df	p		adj p	
score~(1|patient_id)+tp*exp	HAMD	E	Intercept	18.52	0.75	24.66	47.89	<0.001	***	<0.001	***
score~(1|patient_id)+tp*exp	HAMD	E	tp(wk6)	-4.84	0.89	-5.42	26	<0.001	***	<0.001	***
score~(1|patient_id)+tp*exp	HAMD	E	exp	1.36	0.76	1.79	47.89	0.079		0.476	
score~(1|patient_id)+tp*exp	HAMD	E	tp(wk6):exp	-3.91	0.9	-4.34	26	<0.001	***	0.001	**
score~(1|patient_id)+tp*exp	BDI	E	Intercept	28.88	1.7	17	39.62	<0.001	***	<0.001	***
score~(1|patient_id)+tp*exp	BDI	E	tp(wk6)	-10.72	1.6	-6.72	26	<0.001	***	<0.001	***
score~(1|patient_id)+tp*exp	BDI	E	exp	1.58	1.71	0.92	39.62	0.364		1	
score~(1|patient_id)+tp*exp	BDI	E	tp(wk6):exp	-5.47	1.61	-3.4	26	0.002	**	0.013	*
score~(1|patient_id)+tp*exp	MADRS	E	Intercept	27.02	1.24	21.74	48.61	<0.001	***	<0.001	***
score~(1|patient_id)+tp*exp	MADRS	E	tp(wk6)	-6.82	1.51	-4.52	26	<0.001	***	0.001	***
score~(1|patient_id)+tp*exp	MADRS	E	exp	1.25	1.25	0.99	48.61	0.325		1	
score~(1|patient_id)+tp*exp	MADRS	E	tp(wk6):exp	-4.87	1.52	-3.2	26	0.004	**	0.022	*
score~(1|patient_id)+tp*exp	QIDS	E	Intercept	16.72	0.9	18.52	44.31	<0.001	***	<0.001	***
score~(1|patient_id)+tp*exp	QIDS	E	tp(wk6)	-6.43	0.98	-6.59	26	<0.001	***	<0.001	***
score~(1|patient_id)+tp*exp	QIDS	E	exp	0.49	0.91	0.54	44.31	0.593		1	
score~(1|patient_id)+tp*exp	QIDS	E	tp(wk6):exp	-2.46	0.98	-2.5	26	0.019	*	0.115	
score~(1|patient_id)+tp*exp	STAIT	E	Intercept	65.88	1.57	42.06	43.65	<0.001	***	<0.001	***
score~(1|patient_id)+tp*exp	STAIT	E	tp(wk6)	-9.07	1.66	-5.46	26	<0.001	***	<0.001	***
score~(1|patient_id)+tp*exp	STAIT	E	exp	-0.73	1.58	-0.46	43.65	0.645		1	
score~(1|patient_id)+tp*exp	STAIT	E	tp(wk6):exp	-5.2	1.68	-3.1	26	0.005	**	0.028	*
score~(1|patient_id)+tp*exp	WEMWBS	E	Intercept	30.47	1.49	20.39	46.47	<0.001	***	<0.001	***
score~(1|patient_id)+tp*exp	WEMWBS	E	tp(wk6)	6.81	1.72	3.95	24.76	0.001	***	0.003	**
score~(1|patient_id)+tp*exp	WEMWBS	E	exp	-0.64	1.53	-0.42	47.05	0.677		1	
score~(1|patient_id)+tp*exp	WEMWBS	E	tp(wk6):exp	2.95	1.76	1.67	25.2	0.107		0.641	
score~(1|patient_id)+tp*sss	HAMD	E	Intercept	18.7	0.84	22.18	49.08	<0.001	***	<0.001	***
score~(1|patient_id)+tp*sss	HAMD	E	tp(wk6)	-4.74	1.11	-4.28	25	<0.001	***	0.001	**
score~(1|patient_id)+tp*sss	HAMD	E	sss	-0.64	0.82	-0.78	49.08	0.438		1	
score~(1|patient_id)+tp*sss	HAMD	E	tp(wk6):sss	0.9	1.07	0.84	25	0.411		1	
score~(1|patient_id)+tp*sss	BDI	E	Intercept	29.15	1.76	16.53	42.22	<0.001	***	<0.001	***
score~(1|patient_id)+tp*sss	BDI	E	tp(wk6)	-10.62	1.88	-5.64	25	<0.001	***	<0.001	***
score~(1|patient_id)+tp*sss	BDI	E	sss	0.51	1.71	0.3	42.22	0.767		1	
score~(1|patient_id)+tp*sss	BDI	E	tp(wk6):sss	1.03	1.83	0.56	25	0.579		1	
score~(1|patient_id)+tp*sss	MADRS	E	Intercept	27.68	1.31	21.14	46.51	<0.001	***	<0.001	***
score~(1|patient_id)+tp*sss	MADRS	E	tp(wk6)	-7.12	1.58	-4.51	25	<0.001	***	0.001	***
score~(1|patient_id)+tp*sss	MADRS	E	sss	-2.27	1.27	-1.78	46.51	0.081		0.487	
score~(1|patient_id)+tp*sss	MADRS	E	tp(wk6):sss	2.78	1.53	1.81	25	0.082		0.49	
score~(1|patient_id)+tp*sss	QIDS	E	Intercept	16.71	0.96	17.43	42.67	<0.001	***	<0.001	***
score~(1|patient_id)+tp*sss	QIDS	E	tp(wk6)	-6.42	1.04	-6.19	25	<0.001	***	<0.001	***
score~(1|patient_id)+tp*sss	QIDS	E	sss	-0.04	0.93	-0.04	42.67	0.967		1	
score~(1|patient_id)+tp*sss	QIDS	E	tp(wk6):sss	1.08	1.01	1.07	25	0.293		1	
score~(1|patient_id)+tp*sss	STAIT	E	Intercept	65.67	1.63	40.37	42.71	<0.001	***	<0.001	***
score~(1|patient_id)+tp*sss	STAIT	E	tp(wk6)	-8.5	1.76	-4.82	25	<0.001	***	<0.001	***
score~(1|patient_id)+tp*sss	STAIT	E	sss	1.44	1.58	0.91	42.71	0.366		1	
score~(1|patient_id)+tp*sss	STAIT	E	tp(wk6):sss	1.1	1.71	0.64	25	0.525		1	
score~(1|patient_id)+tp*sss	WEMWBS	E	Intercept	30.18	1.51	20.05	42.08	<0.001	***	<0.001	***
score~(1|patient_id)+tp*sss	WEMWBS	E	tp(wk6)	6.6	1.6	4.12	25	<0.001	***	0.002	**
score~(1|patient_id)+tp*sss	WEMWBS	E	sss	1.99	1.46	1.36	42.08	0.18		1	
score~(1|patient_id)+tp*sss	WEMWBS	E	tp(wk6):sss	-2.78	1.55	-1.79	25	0.086		0.516	
score~(1|patient_id)+tp*abs	HAMD	E	Intercept	18.4	0.84	21.87	53.76	<0.001	***	<0.001	***
score~(1|patient_id)+tp*abs	HAMD	E	tp(wk6)	-4.89	1.15	-4.25	27	<0.001	***	0.001	**
score~(1|patient_id)+tp*abs	HAMD	E	abs	0.06	0.84	0.07	53.76	0.946		1	
score~(1|patient_id)+tp*abs	HAMD	E	tp(wk6):abs	0.16	1.14	0.14	27	0.891		1	
score~(1|patient_id)+tp*abs	BDI	E	Intercept	28.76	1.77	16.28	45.35	<0.001	***	<0.001	***
score~(1|patient_id)+tp*abs	BDI	E	tp(wk6)	-10.65	1.87	-5.68	27	<0.001	***	<0.001	***
score~(1|patient_id)+tp*abs	BDI	E	abs	-0.39	1.76	-0.22	45.35	0.823		1	
score~(1|patient_id)+tp*abs	BDI	E	tp(wk6):abs	-1.05	1.86	-0.56	27	0.578		1	
score~(1|patient_id)+tp*abs	MADRS	E	Intercept	26.93	1.36	19.82	52.7	<0.001	***	<0.001	***
score~(1|patient_id)+tp*abs	MADRS	E	tp(wk6)	-7.1	1.76	-4.03	27	<0.001	***	0.002	**
score~(1|patient_id)+tp*abs	MADRS	E	abs	-0.37	1.35	-0.28	52.7	0.784		1	
score~(1|patient_id)+tp*abs	MADRS	E	tp(wk6):abs	0.4	1.75	0.23	27	0.819		1	
score~(1|patient_id)+tp*abs	QIDS	E	Intercept	16.41	0.96	17.15	46.46	<0.001	***	<0.001	***
score~(1|patient_id)+tp*abs	QIDS	E	tp(wk6)	-6.21	1.05	-5.94	27	<0.001	***	<0.001	***
score~(1|patient_id)+tp*abs	QIDS	E	abs	0.24	0.95	0.25	46.46	0.801		1	
score~(1|patient_id)+tp*abs	QIDS	E	tp(wk6):abs	-0.99	1.04	-0.95	27	0.35		1	
score~(1|patient_id)+tp*abs	STAIT	E	Intercept	65.63	1.75	37.49	46.26	<0.001	***	<0.001	***
score~(1|patient_id)+tp*abs	STAIT	E	tp(wk6)	-8.96	1.9	-4.71	27	<0.001	***	<0.001	***
score~(1|patient_id)+tp*abs	STAIT	E	abs	-0.06	1.74	-0.03	46.26	0.975		1	
score~(1|patient_id)+tp*abs	STAIT	E	tp(wk6):abs	-0.03	1.89	-0.02	27	0.986		1	
score~(1|patient_id)+tp*abs	WEMWBS	E	Intercept	30.42	1.47	20.67	50.13	<0.001	***	<0.001	***
score~(1|patient_id)+tp*abs	WEMWBS	E	tp(wk6)	6.75	1.78	3.78	26.44	0.001	***	0.005	**
score~(1|patient_id)+tp*abs	WEMWBS	E	abs	2.17	1.44	1.51	49.75	0.137		0.825	
score~(1|patient_id)+tp*abs	WEMWBS	E	tp(wk6):abs	0.49	1.75	0.28	26.02	0.781		1	

Supplementary table 2: escitalopram treatment's within-arm models of *expectation* (exp) / *suggestibility* (sss) and *absorption* (abs). P-values in the 'adj. p' column have been adjusted for multiple comparisons with the Bonferroni method. All results should be understood as representative at the median level of the covariate and estimates represent the change associated with an increase of 1 standard deviation, see Statistical models for further details.

model	scale	trt	component	estimate	SE	t	df	p		adj p	
score~(1|patient_id)+tp*exp	HAMD	P	Intercept	19.17	0.74	25.75	48.83	<0.001	***	<0.001	***
score~(1|patient_id)+tp*exp	HAMD	P	tp(wk6)	-11.06	1.03	-10.76	24.92	<0.001	***	<0.001	***
score~(1|patient_id)+tp*exp	HAMD	P	exp	-0.08	0.75	-0.11	48.83	0.912		1	
score~(1|patient_id)+tp*exp	HAMD	P	tp(wk6):exp	1.16	1.05	1.1	25.95	0.279		1	
score~(1|patient_id)+tp*exp	BDI	P	Intercept	28.68	1.7	16.87	50	<0.001	***	<0.001	***
score~(1|patient_id)+tp*exp	BDI	P	tp(wk6)	-18.66	2.4	-7.78	25	<0.001	***	<0.001	***
score~(1|patient_id)+tp*exp	BDI	P	exp	-0.48	1.7	-0.28	50	0.779		1	
score~(1|patient_id)+tp*exp	BDI	P	tp(wk6):exp	1.14	2.4	0.47	25	0.64		1	
score~(1|patient_id)+tp*exp	MADRS	P	Intercept	27.73	1.33	20.85	48.19	<0.001	***	<0.001	***
score~(1|patient_id)+tp*exp	MADRS	P	tp(wk6)	-15.14	1.76	-8.59	24.93	<0.001	***	<0.001	***
score~(1|patient_id)+tp*exp	MADRS	P	exp	0.5	1.33	0.37	48.19	0.71		1	
score~(1|patient_id)+tp*exp	MADRS	P	tp(wk6):exp	1.69	1.81	0.94	25.94	0.358		1	
score~(1|patient_id)+tp*exp	QIDS	P	Intercept	14.29	0.95	15.12	49.17	<0.001	***	<0.001	***
score~(1|patient_id)+tp*exp	QIDS	P	tp(wk6)	-7.67	1.25	-6.15	25	<0.001	***	<0.001	***
score~(1|patient_id)+tp*exp	QIDS	P	exp	-0.03	0.95	-0.03	49.17	0.972		1	
score~(1|patient_id)+tp*exp	QIDS	P	tp(wk6):exp	0.56	1.25	0.45	25	0.657		1	
score~(1|patient_id)+tp*exp	STAIT	P	Intercept	64.05	1.88	34.03	50	<0.001	***	<0.001	***
score~(1|patient_id)+tp*exp	STAIT	P	tp(wk6)	-16.69	2.66	-6.27	50	<0.001	***	<0.001	***
score~(1|patient_id)+tp*exp	STAIT	P	exp	2.02	1.88	1.07	50	0.288		1	
score~(1|patient_id)+tp*exp	STAIT	P	tp(wk6):exp	0.64	2.66	0.24	50	0.812		1	
score~(1|patient_id)+tp*exp	WEMWBS	P	Intercept	28.64	1.83	15.67	47.92	<0.001	***	<0.001	***
score~(1|patient_id)+tp*exp	WEMWBS	P	tp(wk6)	16.07	2.47	6.5	24.11	<0.001	***	<0.001	***
score~(1|patient_id)+tp*exp	WEMWBS	P	exp	-0.88	1.78	-0.49	47.9	0.625		1	
score~(1|patient_id)+tp*exp	WEMWBS	P	tp(wk6):exp	-2.96	2.44	-1.21	23.48	0.237		1	
score~(1|patient_id)+tp*sss	HAMD	P	Intercept	19.14	0.67	28.53	49.56	<0.001	***	<0.001	***
score~(1|patient_id)+tp*sss	HAMD	P	tp(wk6)	-10.62	0.92	-11.54	26.06	<0.001	***	<0.001	***
score~(1|patient_id)+tp*sss	HAMD	P	sss	0.08	0.68	0.12	49.56	0.903		1	
score~(1|patient_id)+tp*sss	HAMD	P	tp(wk6):sss	-3.46	0.92	-3.76	25.65	0.001	***	0.005	**
score~(1|patient_id)+tp*sss	BDI	P	Intercept	29.17	1.53	19.04	49.75	<0.001	***	<0.001	***
score~(1|patient_id)+tp*sss	BDI	P	tp(wk6)	-18.1	1.92	-9.42	26	<0.001	***	<0.001	***
score~(1|patient_id)+tp*sss	BDI	P	sss	0.34	1.54	0.22	49.75	0.824		1	
score~(1|patient_id)+tp*sss	BDI	P	tp(wk6):sss	-7.16	1.94	-3.69	26	0.001	**	0.006	**
score~(1|patient_id)+tp*sss	MADRS	P	Intercept	27.89	1.2	23.31	43.98	<0.001	***	<0.001	***
score~(1|patient_id)+tp*sss	MADRS	P	tp(wk6)	-14.46	1.37	-10.53	24.92	<0.001	***	<0.001	***
score~(1|patient_id)+tp*sss	MADRS	P	sss	0.18	1.21	0.15	43.98	0.883		1	
score~(1|patient_id)+tp*sss	MADRS	P	tp(wk6):sss	-6.36	1.37	-4.65	24.58	<0.001	***	0.001	***
score~(1|patient_id)+tp*sss	QIDS	P	Intercept	14.84	0.82	18.07	49.7	<0.001	***	<0.001	***
score~(1|patient_id)+tp*sss	QIDS	P	tp(wk6)	-7.79	1.03	-7.57	26	<0.001	***	<0.001	***
score~(1|patient_id)+tp*sss	QIDS	P	sss	-0.46	0.83	-0.56	49.7	0.578		1	
score~(1|patient_id)+tp*sss	QIDS	P	tp(wk6):sss	-3.31	1.04	-3.19	26	0.004	**	0.022	*
score~(1|patient_id)+tp*sss	STAIT	P	Intercept	64.4	1.61	39.96	50.56	<0.001	***	<0.001	***
score~(1|patient_id)+tp*sss	STAIT	P	tp(wk6)	-16.67	2.08	-8.02	26	<0.001	***	<0.001	***
score~(1|patient_id)+tp*sss	STAIT	P	sss	2.11	1.63	1.3	50.56	0.2		1	
score~(1|patient_id)+tp*sss	STAIT	P	tp(wk6):sss	-9.64	2.1	-4.6	26	<0.001	***	0.001	***
score~(1|patient_id)+tp*sss	WEMWBS	P	Intercept	28.57	1.54	18.55	50.73	<0.001	***	<0.001	***
score~(1|patient_id)+tp*sss	WEMWBS	P	tp(wk6)	15.94	2	7.98	26	<0.001	***	<0.001	***
score~(1|patient_id)+tp*sss	WEMWBS	P	sss	0.14	1.55	0.09	50.73	0.929		1	
score~(1|patient_id)+tp*sss	WEMWBS	P	tp(wk6):sss	6.44	2.02	3.2	26	0.004	**	0.022	*
score~(1|patient_id)+tp*abs	HAMD	P	Intercept	19.21	0.75	25.72	53.83	<0.001	***	<0.001	***
score~(1|patient_id)+tp*abs	HAMD	P	tp(wk6)	-10.42	1.04	-9.99	28.14	<0.001	***	<0.001	***
score~(1|patient_id)+tp*abs	HAMD	P	abs	-0.04	0.74	-0.05	53.83	0.958		1	
score~(1|patient_id)+tp*abs	HAMD	P	tp(wk6):abs	-2.02	1.02	-1.99	27.59	0.056		0.338	
score~(1|patient_id)+tp*abs	BDI	P	Intercept	28.93	1.63	17.77	54.63	<0.001	***	<0.001	***
score~(1|patient_id)+tp*abs	BDI	P	tp(wk6)	-17.25	2.11	-8.17	28	<0.001	***	<0.001	***
score~(1|patient_id)+tp*abs	BDI	P	abs	0.63	1.6	0.39	54.63	0.696		1	
score~(1|patient_id)+tp*abs	BDI	P	tp(wk6):abs	-5.19	2.08	-2.5	28	0.019	*	0.112	
score~(1|patient_id)+tp*abs	MADRS	P	Intercept	27.98	1.35	20.78	51.14	<0.001	***	<0.001	***
score~(1|patient_id)+tp*abs	MADRS	P	tp(wk6)	-14.12	1.69	-8.34	27.26	<0.001	***	<0.001	***
score~(1|patient_id)+tp*abs	MADRS	P	abs	-0.23	1.33	-0.17	51.14	0.863		1	
score~(1|patient_id)+tp*abs	MADRS	P	tp(wk6):abs	-3.45	1.65	-2.1	26.75	0.046	*	0.274	
score~(1|patient_id)+tp*abs	QIDS	P	Intercept	14.67	0.9	16.36	53.55	<0.001	***	<0.001	***
score~(1|patient_id)+tp*abs	QIDS	P	tp(wk6)	-7.29	1.12	-6.48	28	<0.001	***	<0.001	***
score~(1|patient_id)+tp*abs	QIDS	P	abs	-0.63	0.88	-0.72	53.55	0.476		1	
score~(1|patient_id)+tp*abs	QIDS	P	tp(wk6):abs	-1.69	1.11	-1.52	28	0.139		0.831	
score~(1|patient_id)+tp*abs	STAIT	P	Intercept	64.07	1.84	34.91	56	<0.001	***	<0.001	***
score~(1|patient_id)+tp*abs	STAIT	P	tp(wk6)	-16.07	2.6	-6.19	56	<0.001	***	<0.001	***
score~(1|patient_id)+tp*abs	STAIT	P	abs	1.05	1.81	0.58	56	0.562		1	
score~(1|patient_id)+tp*abs	STAIT	P	tp(wk6):abs	-4.82	2.55	-1.89	56	0.064		0.387	
score~(1|patient_id)+tp*abs	WEMWBS	P	Intercept	28.47	1.73	16.47	53.52	<0.001	***	<0.001	***
score~(1|patient_id)+tp*abs	WEMWBS	P	tp(wk6)	15.46	2.27	6.82	27.01	<0.001	***	<0.001	***
score~(1|patient_id)+tp*abs	WEMWBS	P	abs	0.6	1.66	0.36	53.4	0.721		1	
score~(1|patient_id)+tp*abs	WEMWBS	P	tp(wk6):abs	4.1	2.2	1.86	26.31	0.073		0.441	

Supplementary table 3: psilocybin treatment's within-arm models of expectation (exp) / suggestibility (sss) and absorption (abs). P-values in the 'adj. p' column have been adjusted for multiple comparisons with the Bonferroni method. All results should be understood as representative at the median level of the covariate and estimates represent the change associated with an increase of 1 standard deviation, see Statistical models for further details.

model	scale	component	estimate	SE	t	df	p		adj p	
score~(1|patient_id)+tp*trt*exp	HAMD	Intercept	19.8	1.02	19.31	97.79	<0.001	***	<0.001	***
score~(1|patient_id)+tp*trt*exp	HAMD	tp(wk6)	-8.52	1.31	-6.5	50.55	<0.001	***	<0.001	***
score~(1|patient_id)+tp*trt*exp	HAMD	trt(P)	-0.58	1.3	-0.45	97.79	0.653		1	
score~(1|patient_id)+tp*trt*exp	HAMD	exp	1.63	0.89	1.82	97.79	0.071		0.428	
score~(1|patient_id)+tp*trt*exp	HAMD	tp(wk6):trt(P)	-3.06	1.67	-1.83	51.37	0.073		0.438	
score~(1|patient_id)+tp*trt*exp	HAMD	tp(wk6):exp	-4.68	1.14	-4.11	50.55	<0.001	***	0.001	***
score~(1|patient_id)+tp*trt*exp	HAMD	trt(P):exp	-1.72	1.26	-1.37	97.79	0.174		1	
score~(1|patient_id)+tp*trt*exp	HAMD	tp(wk6):trt(P):exp	6.02	1.63	3.68	51.9	0.001	***	0.003	**
score~(1|patient_id)+tp*trt*exp	BDI	Intercept	30.36	2.33	13.04	93.84	<0.001	***	<0.001	***
score~(1|patient_id)+tp*trt*exp	BDI	tp(wk6)	-15.87	2.76	-5.74	51	<0.001	***	<0.001	***
score~(1|patient_id)+tp*trt*exp	BDI	trt(P)	-1.46	2.94	-0.5	93.84	0.62		1	
score~(1|patient_id)+tp*trt*exp	BDI	exp	1.89	2.03	0.93	93.84	0.354		1	
score~(1|patient_id)+tp*trt*exp	BDI	tp(wk6):trt(P)	-3.32	3.49	-0.95	51	0.347		1	
score~(1|patient_id)+tp*trt*exp	BDI	tp(wk6):exp	-6.55	2.41	-2.72	51	0.009	**	0.053	
score~(1|patient_id)+tp*trt*exp	BDI	trt(P):exp	-2.45	2.86	-0.86	93.84	0.394		1	
score~(1|patient_id)+tp*trt*exp	BDI	tp(wk6):trt(P):exp	7.88	3.39	2.32	51	0.024	*	0.146	
score~(1|patient_id)+tp*trt*exp	MADRS	Intercept	28.19	1.76	16.01	97.29	<0.001	***	<0.001	***
score~(1|patient_id)+tp*trt*exp	MADRS	tp(wk6)	-11.39	2.23	-5.11	50.58	<0.001	***	<0.001	***
score~(1|patient_id)+tp*trt*exp	MADRS	trt(P)	-0.68	2.22	-0.31	97.29	0.759		1	
score~(1|patient_id)+tp*trt*exp	MADRS	exp	1.49	1.53	0.97	97.29	0.333		1	
score~(1|patient_id)+tp*trt*exp	MADRS	tp(wk6):trt(P)	-4.52	2.85	-1.59	51.4	0.119		0.711	
score~(1|patient_id)+tp*trt*exp	MADRS	tp(wk6):exp	-5.82	1.94	-3	50.58	0.004	**	0.025	*
score~(1|patient_id)+tp*trt*exp	MADRS	trt(P):exp	-0.91	2.16	-0.42	97.29	0.675		1	
score~(1|patient_id)+tp*trt*exp	MADRS	tp(wk6):trt(P):exp	7.79	2.78	2.8	51.93	0.007	**	0.043	*
score~(1|patient_id)+tp*trt*exp	QIDS	Intercept	17.18	1.27	13.58	94.91	<0.001	***	<0.001	***
score~(1|patient_id)+tp*trt*exp	QIDS	tp(wk6)	-8.74	1.53	-5.73	51	<0.001	***	<0.001	***
score~(1|patient_id)+tp*trt*exp	QIDS	trt(P)	-2.88	1.6	-1.8	94.91	0.075		0.451	
score~(1|patient_id)+tp*trt*exp	QIDS	exp	0.59	1.1	0.53	94.91	0.595		1	
score~(1|patient_id)+tp*trt*exp	QIDS	tp(wk6):trt(P)	0.82	1.93	0.42	51	0.674		1	
score~(1|patient_id)+tp*trt*exp	QIDS	tp(wk6):exp	-2.94	1.33	-2.22	51	0.031	*	0.186	
score~(1|patient_id)+tp*trt*exp	QIDS	trt(P):exp	-0.63	1.55	-0.4	94.91	0.688		1	
score~(1|patient_id)+tp*trt*exp	QIDS	tp(wk6):trt(P):exp	3.6	1.87	1.92	51	0.06		0.361	
score~(1|patient_id)+tp*trt*exp	STAIT	Intercept	65.19	2.36	27.6	100.14	<0.001	***	<0.001	***
score~(1|patient_id)+tp*trt*exp	STAIT	tp(wk6)	-13.96	3.11	-4.5	51	<0.001	***	<0.001	***
score~(1|patient_id)+tp*trt*exp	STAIT	trt(P)	-2.08	2.98	-0.7	100.14	0.489		1	
score~(1|patient_id)+tp*trt*exp	STAIT	exp	-0.88	2.06	-0.43	100.14	0.67		1	
score~(1|patient_id)+tp*trt*exp	STAIT	tp(wk6):trt(P)	-3.03	3.92	-0.77	51	0.444		1	
score~(1|patient_id)+tp*trt*exp	STAIT	tp(wk6):exp	-6.22	2.7	-2.3	51	0.025	*	0.153	
score~(1|patient_id)+tp*trt*exp	STAIT	trt(P):exp	3.24	2.9	1.12	100.14	0.266		1	
score~(1|patient_id)+tp*trt*exp	STAIT	tp(wk6):trt(P):exp	6.96	3.81	1.83	51	0.074		0.441	
score~(1|patient_id)+tp*trt*exp	WEMWBS	Intercept	29.89	2.21	13.53	96.15	<0.001	***	<0.001	***
score~(1|patient_id)+tp*trt*exp	WEMWBS	tp(wk6)	9.56	2.84	3.36	47.39	0.002	**	0.009	**
score~(1|patient_id)+tp*trt*exp	WEMWBS	trt(P)	-0.79	2.82	-0.28	96.39	0.78		1	
score~(1|patient_id)+tp*trt*exp	WEMWBS	exp	-0.64	1.99	-0.32	96.89	0.748		1	
score~(1|patient_id)+tp*trt*exp	WEMWBS	tp(wk6):trt(P)	7.82	3.61	2.16	47.93	0.036	*	0.214	
score~(1|patient_id)+tp*trt*exp	WEMWBS	tp(wk6):exp	3.4	2.53	1.35	49.18	0.185		1	
score~(1|patient_id)+tp*trt*exp	WEMWBS	trt(P):exp	-0.43	2.78	-0.16	96.68	0.877		1	
score~(1|patient_id)+tp*trt*exp	WEMWBS	tp(wk6):trt(P):exp	-6.82	3.54	-1.92	48.62	0.06		0.361	

Supplementary table 4: between-arm models adjusted for expectancy. P-values in the 'adj. p' column have been adjusted for multiple comparisons with the Bonferroni method. All results should be understood as representative at the median level of the covariate and estimates represent the change associated with an increase of 1 standard deviation, see Statistical models for further details.

model	scale	component	estimate	SE	t	df	p		adj p	
score~(1|patient_id)+tp*trt*sss	HAMD	Intercept	18.7	0.78	23.99	98.63	<0.001	***	<0.001	***
score~(1|patient_id)+tp*trt*sss	HAMD	tp(wk6)	-4.74	1.03	-4.58	50.11	<0.001	***	<0.001	***
score~(1|patient_id)+tp*trt*sss	HAMD	trt(P)	0.44	1.07	0.41	98.63	0.682		1	
score~(1|patient_id)+tp*trt*sss	HAMD	sss	-0.65	0.77	-0.85	98.63	0.399		1	
score~(1|patient_id)+tp*trt*sss	HAMD	tp(wk6):trt(P)	-5.88	1.44	-4.09	51.04	<0.001	***	0.001	***
score~(1|patient_id)+tp*trt*sss	HAMD	tp(wk6):sss	0.92	1.02	0.9	50.11	0.374		1	
score~(1|patient_id)+tp*trt*sss	HAMD	trt(P):sss	0.73	1.06	0.69	98.63	0.492		1	
score~(1|patient_id)+tp*trt*sss	HAMD	tp(wk6):trt(P):sss	-4.34	1.42	-3.06	50.66	0.004	**	0.021	*
score~(1|patient_id)+tp*trt*sss	BDI	Intercept	29.15	1.69	17.22	92.09	<0.001	***	<0.001	***
score~(1|patient_id)+tp*trt*sss	BDI	tp(wk6)	-10.62	1.96	-5.41	51	<0.001	***	<0.001	***
score~(1|patient_id)+tp*trt*sss	BDI	trt(P)	0.02	2.33	0.01	92.09	0.995		1	
score~(1|patient_id)+tp*trt*sss	BDI	sss	0.52	1.67	0.31	92.09	0.757		1	
score~(1|patient_id)+tp*trt*sss	BDI	tp(wk6):trt(P)	-7.48	2.7	-2.77	51	0.008	**	0.047	*
score~(1|patient_id)+tp*trt*sss	BDI	tp(wk6):sss	1.05	1.94	0.54	51	0.591		1	
score~(1|patient_id)+tp*trt*sss	BDI	trt(P):sss	-0.18	2.31	-0.08	92.09	0.939		1	
score~(1|patient_id)+tp*trt*sss	BDI	tp(wk6):trt(P):sss	-8.12	2.68	-3.03	51	0.004	**	0.023	*
score~(1|patient_id)+tp*trt*sss	MADRS	Intercept	27.68	1.29	21.49	90.75	<0.001	***	<0.001	***
score~(1|patient_id)+tp*trt*sss	MADRS	tp(wk6)	-7.12	1.5	-4.75	49.16	<0.001	***	<0.001	***
score~(1|patient_id)+tp*trt*sss	MADRS	trt(P)	0.21	1.77	0.12	90.75	0.906		1	
score~(1|patient_id)+tp*trt*sss	MADRS	sss	-2.31	1.27	-1.81	90.75	0.073		0.439	
score~(1|patient_id)+tp*trt*sss	MADRS	tp(wk6):trt(P)	-7.36	2.09	-3.52	50	0.001	***	0.006	**
score~(1|patient_id)+tp*trt*sss	MADRS	tp(wk6):sss	2.83	1.48	1.91	49.16	0.062		0.373	
score~(1|patient_id)+tp*trt*sss	MADRS	trt(P):sss	2.48	1.76	1.41	90.75	0.161		0.967	
score~(1|patient_id)+tp*trt*sss	MADRS	tp(wk6):trt(P):sss	-9.12	2.06	-4.42	49.65	<0.001	***	<0.001	***
score~(1|patient_id)+tp*trt*sss	QIDS	Intercept	16.71	0.91	18.28	92.38	<0.001	***	<0.001	***
score~(1|patient_id)+tp*trt*sss	QIDS	tp(wk6)	-6.42	1.06	-6.03	51	<0.001	***	<0.001	***
score~(1|patient_id)+tp*trt*sss	QIDS	trt(P)	-1.88	1.26	-1.49	92.38	0.139		0.832	
score~(1|patient_id)+tp*trt*sss	QIDS	sss	-0.04	0.9	-0.04	92.38	0.966		1	
score~(1|patient_id)+tp*trt*sss	QIDS	tp(wk6):trt(P)	-1.37	1.46	-0.94	51	0.353		1	
score~(1|patient_id)+tp*trt*sss	QIDS	tp(wk6):sss	1.1	1.05	1.05	51	0.3		1	
score~(1|patient_id)+tp*trt*sss	QIDS	trt(P):sss	-0.42	1.25	-0.34	92.38	0.737		1	
score~(1|patient_id)+tp*trt*sss	QIDS	tp(wk6):trt(P):sss	-4.37	1.45	-3.01	51	0.004	**	0.024	*
score~(1|patient_id)+tp*trt*sss	STAIT	Intercept	65.67	1.67	39.38	94.46	<0.001	***	<0.001	***
score~(1|patient_id)+tp*trt*sss	STAIT	tp(wk6)	-8.5	2	-4.25	51	<0.001	***	0.001	***
score~(1|patient_id)+tp*trt*sss	STAIT	trt(P)	-1.27	2.29	-0.55	94.46	0.582		1	
score~(1|patient_id)+tp*trt*sss	STAIT	sss	1.47	1.65	0.89	94.46	0.375		1	
score~(1|patient_id)+tp*trt*sss	STAIT	tp(wk6):trt(P)	-8.17	2.75	-2.97	51	0.004	**	0.027	*
score~(1|patient_id)+tp*trt*sss	STAIT	tp(wk6):sss	1.12	1.97	0.57	51	0.572		1	
score~(1|patient_id)+tp*trt*sss	STAIT	trt(P):sss	0.61	2.28	0.27	94.46	0.788		1	
score~(1|patient_id)+tp*trt*sss	STAIT	tp(wk6):trt(P):sss	-10.66	2.73	-3.91	51	<0.001	***	0.002	**
score~(1|patient_id)+tp*trt*sss	WEMWBS	Intercept	30.18	1.57	19.22	94.48	<0.001	***	<0.001	***
score~(1|patient_id)+tp*trt*sss	WEMWBS	tp(wk6)	6.6	1.88	3.51	51	0.001	***	0.006	**
score~(1|patient_id)+tp*trt*sss	WEMWBS	trt(P)	-1.61	2.16	-0.75	94.48	0.458		1	
score~(1|patient_id)+tp*trt*sss	WEMWBS	sss	2.03	1.55	1.31	94.48	0.194		1	
score~(1|patient_id)+tp*trt*sss	WEMWBS	tp(wk6):trt(P)	9.34	2.59	3.61	51	0.001	***	0.004	**
score~(1|patient_id)+tp*trt*sss	WEMWBS	tp(wk6):sss	-2.83	1.86	-1.52	51	0.134		0.806	
score~(1|patient_id)+tp*trt*sss	WEMWBS	trt(P):sss	-1.89	2.14	-0.88	94.48	0.38		1	
score~(1|patient_id)+tp*trt*sss	WEMWBS	tp(wk6):trt(P):sss	9.2	2.57	3.58	51	0.001	***	0.005	**

Supplementary table 5: between-arm models adjusted for suggestibility. P-values in the ‘adj. p’ column have been adjusted for multiple comparisons with the Bonferroni method. All results should be understood as representative at the median level of the covariate and estimates represent the change associated with an increase of 1 standard deviation, see Statistical models for further details.

model	component	arm	scale	Eq. bound	p		adj p
score~(1|patient_id)+tp*exp	tp:exp	P	HAMD	2.3	0.214		1
score~(1|patient_id)+tp*exp	tp:exp	P	BDI	4.7	0.131		0.786
score~(1|patient_id)+tp*exp	tp:exp	P	MADRS	3.9	0.192		1
score~(1|patient_id)+tp*exp	tp:exp	P	QIDS	2.6	0.112		0.672
score~(1|patient_id)+tp*exp	tp:exp	P	STAIT	5.1	0.12		0.72
score~(1|patient_id)+tp*exp	tp:exp	P	WEMWBS	2.5	0.362		1
score~(1|patient_id)+tp*sss	tp:sss	E	HAMD	2.3	0.101		0.606
score~(1|patient_id)+tp*sss	tp:sss	E	BDI	4.7	0.028	*	0.168
score~(1|patient_id)+tp*sss	tp:sss	E	MADRS	3.9	0.255		1
score~(1|patient_id)+tp*sss	tp:sss	E	QIDS	2.6	0.078		0.468
score~(1|patient_id)+tp*sss	tp:sss	E	STAIT	5.1	0.014	*	0.084
score~(1|patient_id)+tp*sss	tp:sss	E	WEMWBS	2.5	0.147		0.882
score~(1|patient_id)+tp*trt*exp	tp:trt	between-arms	HAMD	2.9	0.524		1
score~(1|patient_id)+tp*trt*exp	tp:trt	between-arms	BDI	5.6	0.268		1
score~(1|patient_id)+tp*trt*exp	tp:trt	between-arms	MADRS	4.6	0.484		1
score~(1|patient_id)+tp*trt*exp	tp:trt	between-arms	QIDS	2.9	0.165		0.99
score~(1|patient_id)+tp*trt*exp	tp:trt	between-arms	STAIT	6.2	0.219		1
score~(1|patient_id)+tp*trt*exp	tp:trt	between-arms	WEMWBS	5.4	0.747		1

Supplementary table 6: equivalence testing non-significant results. In all cases the equivalence bound was selected to be 0.5 standardized mean difference (SMD), see Equivalence testing for details, which corresponds to a score difference shown in the 'Eq. bound' column. First 6 rows show equivalnce test results for the lack of expectancy-outcomes assocation in the psilocybin arm, the second 6 rows show equivalnce test results for the lack of suggestibility-outcomes assocation in the escitalopram arm and the last 6 rows show equivalence test results for the lack of a between-treatment difference in the expectancy adjusted models.

scale	component	Between-trt diff. unadjusted models					Between-trt diff. expectancy adjusted models			
		est ± SE	p		adj p		est ± SE	p		adj p
HAMD	tp(wk6):trt(P)	-6.0 ± 1.5	<0.001	***	0.002	**	-3.1 ± 1.7	0.073		0.438
BDI	tp(wk6):trt(P)	-7.6 ± 2.9	0.011	*	0.069		-3.3 ± 3.5	0.347		1
MADRS	tp(wk6):trt(P)	-7.9 ± 2.4	0.002	**	0.013	*	-4.5 ± 2.9	0.119		0.711
QIDS	tp(wk6):trt(P)	-1.3 ± 1.5	0.402		1		0.8 ± 1.9	0.674		1
STAIT	tp(wk6):trt(P)	-8.2 ± 3.3	0.015	*	0.089		-3.0 ± 3.9	0.444		1
WEMWBS	tp(wk6):trt(P)	9.5 ± 2.9	0.002	**	0.01	*	7.8 ± 3.6	0.036	*	0.214

Supplementary Table 7: comparison of between treatment models with and without adjustment for pre-treatment expectancy, see Statistical models for further details.