

FIG. 1A

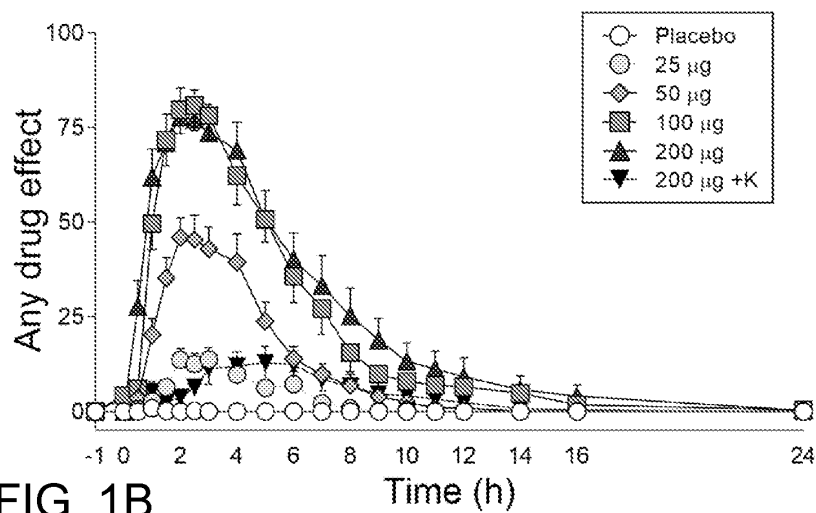


FIG. 1B

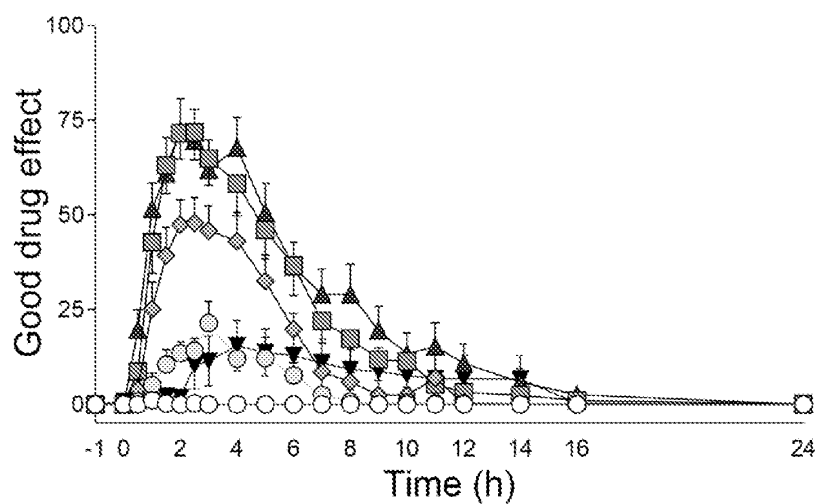


FIG. 1C

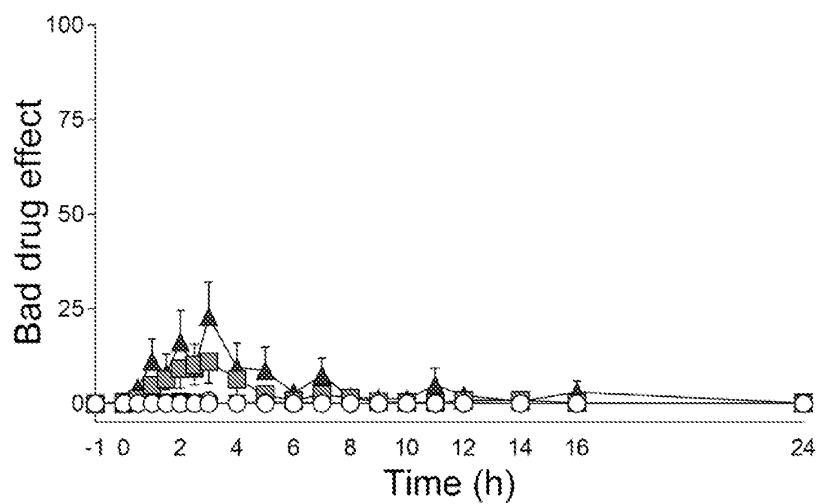


FIG. 1D

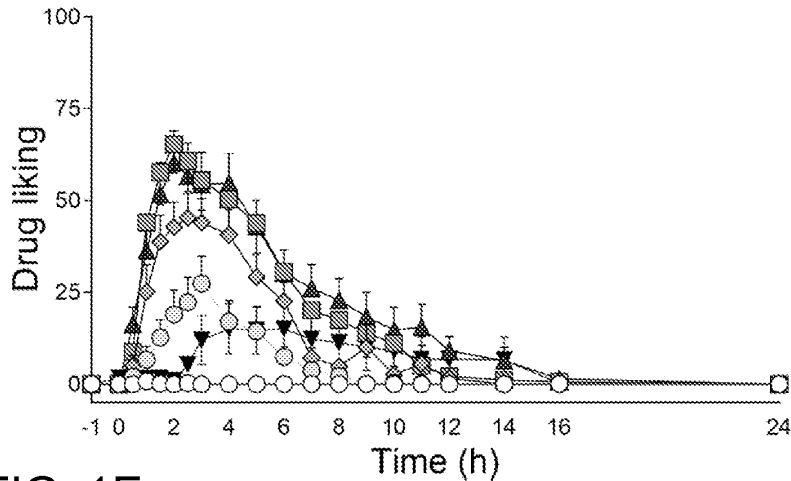


FIG. 1E

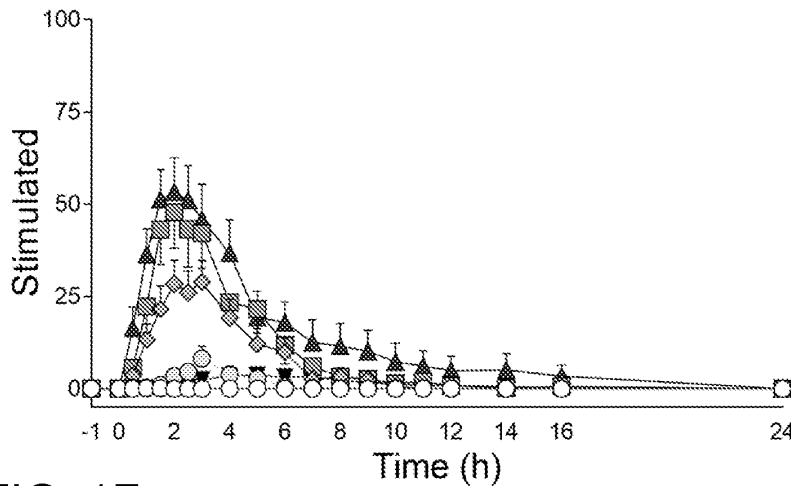


FIG. 1F

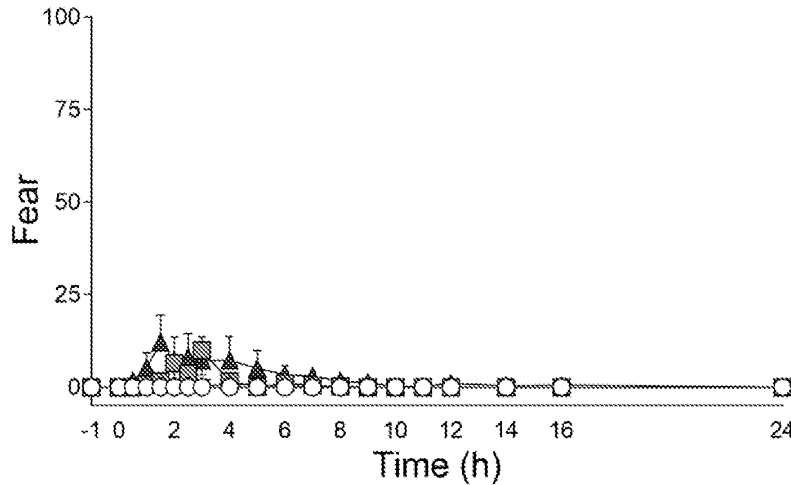


FIG. 1G

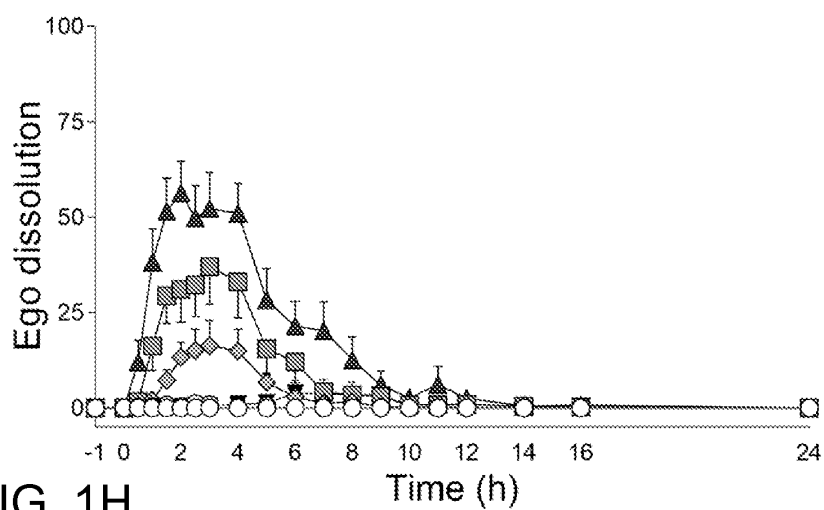


FIG. 1H

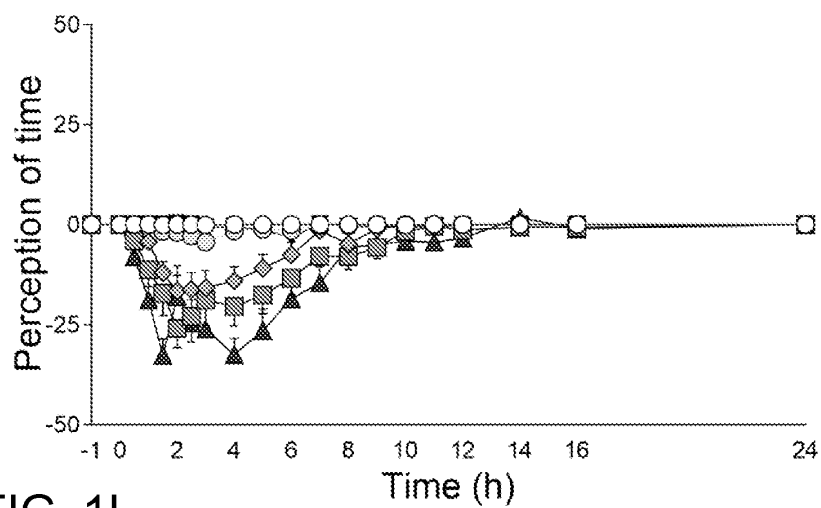
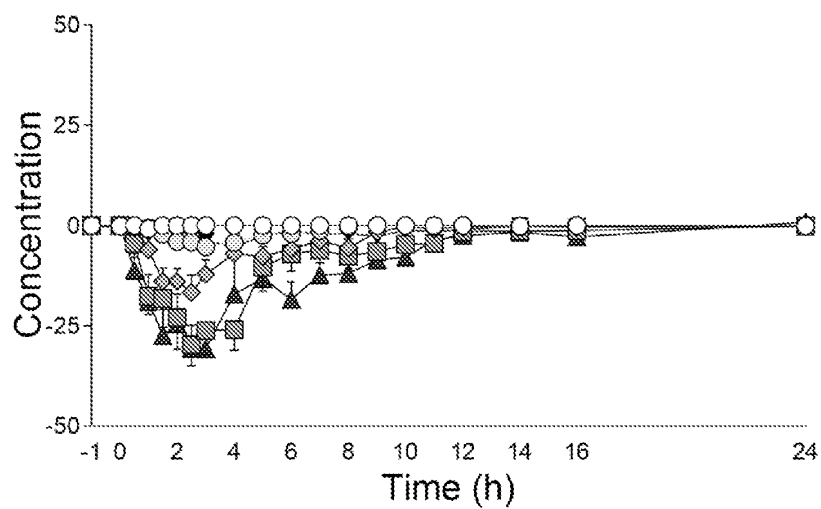


FIG. 1I



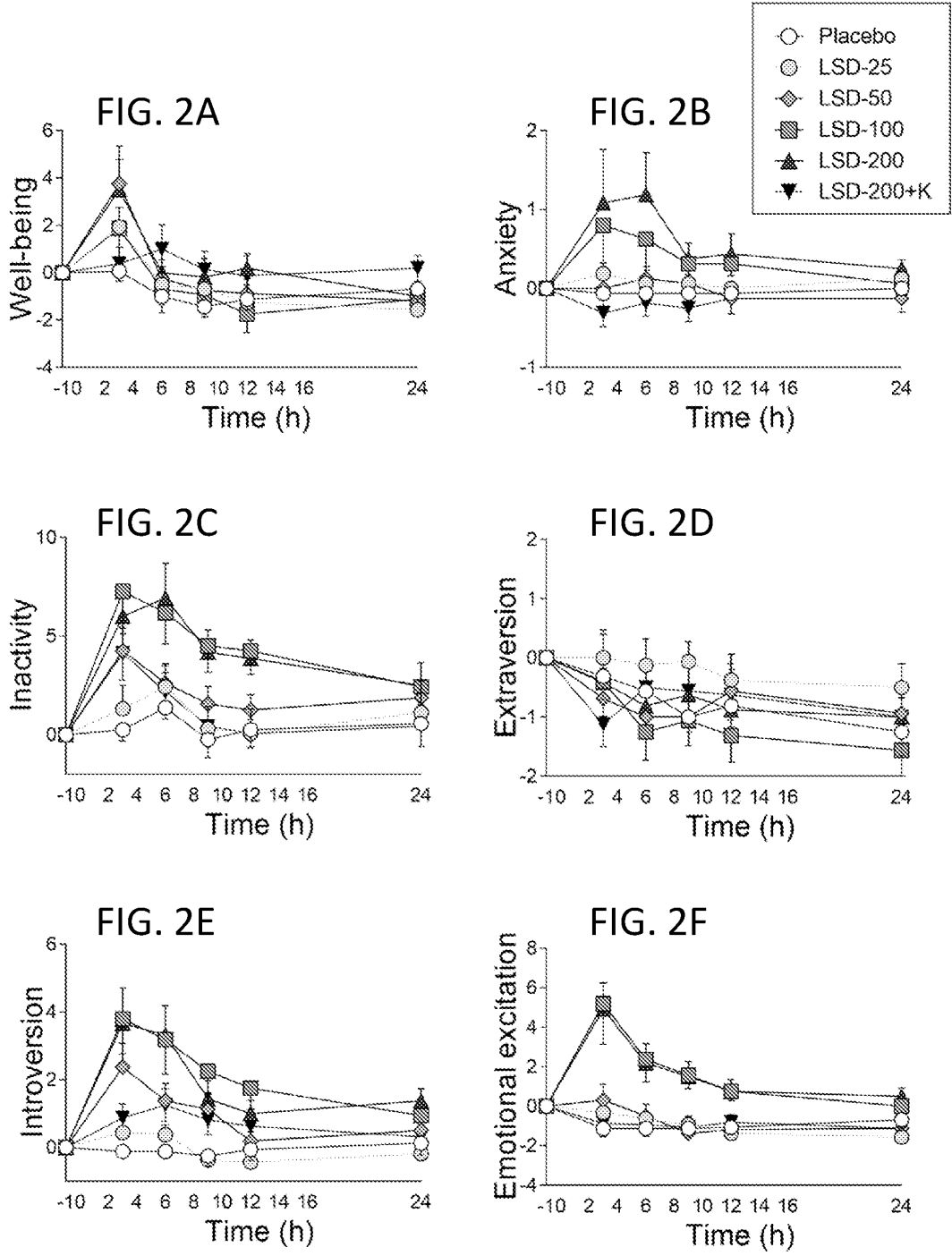


FIG. 3

Mean values and statistics for the acute effects of LSD alone, LSD + ketanserin, and placebo.

		Placebo	LSD 25 µg	LSD 50 µg	LSD 100 µg	LSD 200 µg	LSD 200 µg + Ketanserin	F _{5,75}	P=
		(mean ± SEM)	(mean ± SEM)	(mean ± SEM)	(mean ± SEM)	(mean ± SEM)	(mean ± SEM)		
Subjective effects									
Visual Analogue Scale (VAS, %max)									
Any drug effect	ΔE _{max}	0.9 ± 0.6	20 ± 3.8	57 ± 5.5	86 ± 5.7	83 ± 6.7	22 ± 4.9	72.9	<0.001
	AUEC	0.6 ± 0.4	58 ± 12	205 ± 32	431 ± 51	508 ± 82	133 ± 33	31.2	<0.001
Good drug effect	ΔE _{max}	1.1 ± 0.8	32 ± 6.8	59 ± 6.7	81 ± 6.9	82 ± 6.6	22 ± 6.8	43.3	<0.001
Bad drug effect	ΔE _{max}	0.1 ± 0.1	1.6 ± 0.8	1.5 ± 0.4	17 ± 5.9	28 ± 8.7	1.6 ± 0.6	8.82	<0.001
Drug liking	ΔE _{max}	0.8 ± 0.5	32 ± 7.5	60 ± 6.7	79 ± 8.1	76 ± 7.8	26 ± 7.2	29.5	<0.001
Stimulated	ΔE _{max}	0.1 ± 0.1	9.3 ± 3.3	40 ± 6.4	57 ± 10	66 ± 8.5	8.0 ± 2.4	27.8	<0.001
Fear	ΔE _{max}	0.0 ± 0.0	0.2 ± 0.1	1.2 ± 0.8	11 ± 6.7	15 ± 8.4	0.4 ± 0.3	2.85	<0.05
Ego dissolution	ΔE _{max}	0.0 ± 0.0	1.5 ± 0.7	21 ± 6.7	51 ± 9.6	73 ± 7.5	4.9 ± 3.7	35.6	<0.001
Concentration	ΔE _{max}	0.0 ± 0.0	0.3 ± 0.2	3.4 ± 2.1	11 ± 4.3	11 ± 4.6	1.8 ± 1.1	4.31	<0.01
	ΔE _{min}	-0.8 ± 0.7	-6.4 ± 2.1	-22 ± 3.6	-37 ± 4.8	-44 ± 2.9	-7.8 ± 2.1	50.9	<0.001
Sense of time	ΔE _{max}	0.1 ± 0.1	0.2 ± 0.1	0.7 ± 0.6	3.8 ± 3.0	13 ± 5.0	1.9 ± 1.6	4.54	<0.01
	ΔE _{min}	-0.1 ± 0.1	-5.4 ± 2.2	-25 ± 4.4	-32 ± 4.5	-41 ± 3.3	-3.4 ± 1.8	43.0	<0.001

	Pla - 25 µg	Pla - 50 µg	Pla - 100 µg	Pla - 200 µg	Pla - 200 µg +K	25 µg - 50 µg	25 µg - 100 µg	25 µg - 200 µg	25 µg - 200 µg +K	50 µg - 100 µg	50 µg - 200 µg	50 µg - 200 µg +K	100 µg - 200 µg	100 µg - 200 µg +K	200 µg - 200 µg +K
Subjective effects															
Visual Analogue Scale (VAS, %max)															
Any drug effect	*	***	***	***	*	***	***	***	NS	***	***	***	NS	***	***
AUEC	NS	**	***	***	NS	NS	***	***	NS	***	***	NS	NS	***	***
Good drug effect	***	***	***	***	*	**	***	***	NS	*	*	***	NS	***	***
Bad drug effect	NS	NS	*	***	NS	NS	NS	***	NS	NS	***	NS	NS	NS	***
Drug liking	***	***	***	***	*	*	***	***	NS	NS	NS	***	NS	***	***
Stimulated	NS	***	***	***	NS	**	***	***	NS	NS	*	***	NS	***	***
Fear	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Ego dissolution	NS	*	***	***	NS	NS	***	***	NS	**	***	NS	*	***	***
Concentration	NS	NS	*	*	NS	NS	*	*	NS	NS	NS	NS	NS	NS	NS
ΔE _{min}	NS	***	***	***	NS	***	***	***	NS	**	***	**	NS	***	***
Sense of time	NS	NS	NS	**	NS	NS	NS	**	NS	NS	**	NS	NS	NS	*
ΔE _{min}	NS	***	***	***	NS	***	***	***	NS	NS	***	***	NS	***	***

*P<0.05, **P<0.01, ***P<0.001; NS, not significant; E_{max}, maximal effect; ΔE_{max}, maximal difference from baseline; C_{max}, maximal concentration

FIG. 3 cont'd

		Placebo	LSD 25 µg	LSD 50 µg	LSD 100 µg	LSD 200 µg	LSD 200 µg + Ketanserin	F _{6,78}	P=				
		(mean ± SEM)	(mean ± SEM)	(mean ± SEM)	(mean ± SEM)	(mean ± SEM)	(mean ± SEM)						
5 Dimensions of Altered States of Consciousness (ASC) Scale													
Total ASC score	% score	0.1 ± 0.0	2.2 ± 0.6	9.5 ± 1.8	23 ± 2.9	30 ± 3.2	4.5 ± 1.5	52.0	<0.001				
Oceanic boundlessness	% score	0.0 ± 0.0	2.9 ± 1.0	12 ± 2.8	28 ± 4.7	36 ± 5.1	4.1 ± 2.2	29.3	<0.001				
Anxious ego-dissolution	% score	0.0 ± 0.0	0.6 ± 0.3	3.3 ± 1.1	11 ± 2.6	21 ± 5.4	1.1 ± 0.4	14.0	<0.001				
Visionary restructuring	% score	0.1 ± 0.0	3.1 ± 1.2	18 ± 4.1	43 ± 5.4	50 ± 4.7	7.4 ± 3.1	45.9	<0.001				
Auditory alterations	% score	0.0 ± 0.0	0.4 ± 0.2	2.6 ± 1.0	9.1 ± 3.2	13 ± 3.3	2.5 ± 1.7	8.39	<0.001				
Reductions of vigilance	% score	0.6 ± 0.2	4.5 ± 1.7	12 ± 2.3	24 ± 4.8	27 ± 4.7	10 ± 2.8	16.6	<0.001				
Experience of unity	% score	0.0 ± 0.0	1.1 ± 0.7	10 ± 3.3	26 ± 6.0	40 ± 7.5	3.5 ± 2.6	17.4	<0.001				
Spiritual experience	% score	0.0 ± 0.0	0.9 ± 0.9	4.9 ± 2.4	17 ± 4.5	18 ± 4.1	3.0 ± 1.8	10.9	<0.001				
Blissful state	% score	0.1 ± 0.1	5.6 ± 1.8	18 ± 5.3	34 ± 7.8	33 ± 5.5	5.5 ± 2.6	10.5	<0.001				
Insightfulness	% score	0.0 ± 0.0	3.4 ± 1.8	9.9 ± 3.4	30 ± 6.1	29 ± 5.6	2.2 ± 1.1	17.7	<0.001				
Disembodiment	% score	0.0 ± 0.0	0.1 ± 0.1	3.6 ± 1.5	16 ± 5.8	37 ± 6.9	1.0 ± 0.6	16.9	<0.001				
Impaired control and cognition	% score	0.1 ± 0.1	1.6 ± 0.8	6.6 ± 2.4	19 ± 3.5	27 ± 5.2	2.4 ± 1.0	23.3	<0.001				
Anxiety	% score	0.0 ± 0.0	0.0 ± 0.0	0.5 ± 0.3	6.1 ± 3.0	17 ± 7.7	0.4 ± 0.3	4.51	<0.01				
Complex imagery	% score	0.0 ± 0.0	4.3 ± 2.2	19 ± 6.6	53 ± 8.2	62 ± 8.1	8.8 ± 3.7	28.5	<0.001				
Elementary imagery	% score	0.4 ± 0.3	2.6 ± 1.2	25 ± 6.9	50 ± 5.9	68 ± 6.6	14 ± 6.8	26.8	<0.001				
Audio-visual synesthesia	% score	0.0 ± 0.0	3.1 ± 1.6	25 ± 6.8	58 ± 8.4	70 ± 7.6	12 ± 5.2	28.5	<0.001				
Changed meaning of percepts	% score	0.0 ± 0.0	1.3 ± 0.6	12 ± 3.5	26 ± 8.0	30 ± 5.5	2.6 ± 1.3	12.9	<0.001				
		Pla - 25 µg	Pia - 50 µg	Pia - 100 µg	Pia - 200 µg	Pla - 200 µg +K	25 µg - 200 µg +K	50 µg - 200 µg +K	100 µg - 200 µg +K	200 µg - 200 µg +K			
5 Dimensions of Altered States of Consciousness (ASC) Scale													
Total ASC score	NS	**	***	***	NS	*	***	***	NS	NS	***	***	
Oceanic boundlessness	NS	*	***	***	NS	NS	***	***	NS	NS	***	***	
Anxious ego-dissolution	NS	NS	**	***	NS	NS	*	***	NS	NS	*	***	
Visionary restructuring	NS	**	***	***	NS	*	***	***	NS	NS	***	***	
Auditory alterations	NS	NS	**	***	NS	NS	*	***	NS	NS	NS	**	
Reductions of vigilance	NS	*	***	***	NS	NS	***	***	NS	*	NS	NS	**
Experience of unity	NS	NS	***	***	NS	NS	***	***	NS	*	NS	NS	**
Spiritual experience	NS	NS	***	***	NS	NS	***	***	NS	*	NS	NS	**
Blissful state	NS	NS	***	***	NS	NS	***	***	NS	NS	NS	NS	***
Insightfulness	NS	NS	***	***	NS	NS	***	***	NS	NS	NS	NS	***
Disembodiment	NS	NS	*	***	NS	NS	*	***	NS	NS	***	NS	**
Impaired control and cognition	NS	NS	***	***	NS	NS	***	***	NS	**	NS	NS	***
Anxiety	NS	NS	NS	**	NS	NS	NS	**	NS	NS	**	NS	NS
Complex imagery	NS	NS	***	***	NS	NS	***	***	NS	NS	NS	NS	***
Elementary imagery	NS	*	***	***	NS	*	***	***	NS	*	NS	NS	***
Audio-visual synesthesia	NS	*	***	***	NS	NS	***	***	NS	**	NS	NS	***
Changed meaning of percepts	NS	NS	***	***	NS	NS	***	***	NS	NS	*	NS	NS

*P<0.05, **P<0.01, ***P<0.001; NS, not significant; E_{max}, maximal effect; ΔE_{max}, maximal difference from baseline; C_{max}, maximal concentration

FIG. 3 cont'd

FIG. 3 cont'd

		Placebo	LSD 25 µg	LSD 50 µg	LSD 100 µg	LSD 200 µg	LSD 200 µg + Ketanserin	F _{5,75}	P=				
		(mean ± SEM)	(mean ± SEM)	(mean ± SEM)	(mean ± SEM)	(mean ± SEM)	(mean ± SEM)						
Mystical Effects Questionnaire (MEQ43)													
Internal unity	% score	0.0 ± 0.0	3.8 ± 1.6	14 ± 4.2	28 ± 6.3	38 ± 6.7	7.5 ± 3.7	16.3	<0.001				
External unity	% score	0.0 ± 0.0	3.3 ± 1.9	12.7 ± 3.7	26 ± 5.2	33 ± 5.3	9.8 ± 4.0	18.4	<0.001				
Sacredness	% score	0.0 ± 0.0	6.3 ± 2.4	19.1 ± 4.7	30 ± 6.5	34 ± 6.4	11 ± 4.8	12.1	<0.001				
Noetic quality	% score	1.3 ± 1.3	8.1 ± 3.7	15 ± 3.6	35 ± 6.6	27 ± 5.3	6.6 ± 3.2	16.4	<0.001				
Deeply felt positive mood	% score	0.0 ± 0.0	16 ± 4.1	30 ± 5.7	39 ± 5.9	44 ± 6.4	16 ± 5.6	16.1	<0.001				
Transcendence of time/space	% score	0.0 ± 0.0	6.3 ± 2.0	25 ± 5.0	46 ± 6.5	61 ± 7.0	11 ± 4.4	37.0	<0.001				
Ineffability	% score	0.0 ± 0.0	9.5 ± 4.1	32 ± 5.7	52 ± 4.9	61 ± 5.2	15 ± 5.7	40.3	<0.001				
Mystical Effects Questionnaire (MEQ30)													
Mystical	% score	0.3 ± 0.3	4.4 ± 2.0	14.8 ± 4.2	28 ± 6.4	32 ± 5.7	8.1 ± 3.8	14.4	<0.001				
Positive mood	% score	0.0 ± 0.0	18 ± 4.0	31 ± 5.2	42 ± 5.5	45 ± 6.4	17 ± 5.9	18.8	<0.001				
Transcendence of time/space	% score	0.0 ± 0.0	7.3 ± 2.2	26 ± 4.9	47 ± 6.0	61 ± 6.9	11 ± 4.3	39.9	<0.001				
Ineffability	% score	0.0 ± 0.0	13 ± 5.3	45 ± 7.1	71 ± 5.8	78 ± 6.0	19 ± 6.7	39.6	<0.001				
MEQ30 total score	% score	0.2 ± 0.2	8.5 ± 2.4	23 ± 4.4	39 ± 5.3	45 ± 5.4	12 ± 4.4	30.5	<0.001				
Nadir	% score	0.0 ± 0.0	1.4 ± 0.6	7.6 ± 2.5	14 ± 3.6	26 ± 6.8	4.3 ± 1.6	11.8	<0.001				
Aesthetic Experience	% score	0.5 ± 0.3	8.5 ± 2.78	28 ± 5.2	46 ± 5.8	48 ± 5.7	17 ± 4.2	27.4	<0.001				
		Pla - 25 µg	Pla - 50 µg	Pla - 100 µg	Pla - 200 µg +K	25 µg - 100 µg	25 µg - 200 µg +K	25 µg - 50 µg	50 µg - 200 µg +K	50 µg - 100 µg	100 µg - 200 µg +K	100 µg - 200 µg +K	200 µg - 200 µg +K
Mystical Effects Questionnaire (MEQ43)													
Internal unity		NS	NS	***	***	NS	NS	***	NS	NS	**	***	
External unity		NS	*	***	***	NS	NS	***	NS	*	***	NS	NS
Sacredness		NS	**	***	***	NS	NS	***	NS	NS	NS	NS	NS
Noetic quality		NS	*	***	***	NS	NS	***	NS	***	NS	NS	NS
Deeply felt positive mood		NS	***	***	***	NS	NS	***	NS	NS	NS	NS	NS
Transcendence of time/space		NS	***	***	***	NS	*	***	NS	**	***	NS	NS
Ineffability		NS	***	***	***	NS	**	***	NS	**	***	*	NS
Mystical Effects Questionnaire (MEQ30)													
Mystical		NS	*	***	***	NS	NS	***	NS	NS	**	NS	NS
Positive mood		*	***	***	***	*	NS	***	NS	NS	NS	NS	NS
Transcendence of time/space		NS	***	***	***	NS	**	***	NS	**	***	NS	NS
Ineffability		NS	***	***	***	NS	***	***	NS	**	***	**	NS
MEQ30 total score		NS	***	***	***	NS	*	***	NS	*	***	NS	NS
Nadir		NS	NS	**	***	NS	NS	*	NS	NS	***	NS	*
Aesthetic Experience		NS	***	***	***	*	**	***	NS	*	**	NS	NS

*P<0.05, **P<0.01, ***P<0.001; NS, not significant; E_{max}, maximal effect; ΔE_{max}, maximal difference from baseline; C_{max}, maximal concentration

FIG. 3 cont'd

		Placebo	LSD 25 µg	LSD 50 µg	LSD 100 µg	LSD 200 µg	LSD 200 µg + Ketanserin	$F_{5,75}$	$P=$
		(mean ± SEM)	(mean ± SEM)	(mean ± SEM)	(mean ± SEM)	(mean ± SEM)	(mean ± SEM)		
Adjective Mood Rating Scale (AMRS score)									
Well-being	ΔE_{max}	0.5 ± 0.3	2.6 ± 0.6	4.1 ± 1.0	3.1 ± 1.2	4.0 ± 1.3	2.3 ± 0.8	2.41	<0.05
Anxiety	ΔE_{max}	0.0 ± 0.1	0.3 ± 0.1	0.2 ± 0.2	1.0 ± 0.5	1.8 ± 0.7	0.2 ± 0.2	4.07	<0.01
Inactivity	ΔE_{max}	2.9 ± 0.8	4.3 ± 1.1	6.4 ± 1.0	9.4 ± 2.0	9.6 ± 1.6	5.4 ± 1.3	6.27	<0.001
Extraversion	ΔE_{max}	0.1 ± 0.2	0.8 ± 0.4	0.5 ± 0.4	0.5 ± 0.4	0.8 ± 0.5	0.2 ± 0.3	0.74	NS
Introversion	ΔE_{max}	0.6 ± 0.3	0.8 ± 0.4	3.0 ± 0.7	4.8 ± 1.1	4.3 ± 0.9	1.9 ± 0.6	11.6	<0.001
Emotional excitation	ΔE_{max}	-0.6 ± 0.3	-0.2 ± 0.4	0.9 ± 0.6	5.8 ± 1.9	5.4 ± 1.2	0.1 ± 0.5	9.25	<0.001
Autonomic effects									
Systolic blood pressure (mmHg)	E_{max}	131 ± 3.5	133 ± 3.0	137 ± 3.2	139 ± 3.5	138 ± 2.4	133 ± 3.0	5.05	<0.001
	E_{min}	110 ± 2.7	113 ± 2.9	115 ± 2.3	113 ± 2.9	117 ± 2.2	109 ± 3.0	6.77	<0.001
Diastolic blood pressure (mmHg)	E_{max}	80 ± 2.1	83 ± 1.7	84 ± 1.9	85 ± 2.0	87 ± 2.0	83 ± 1.8	4.76	<0.001
	E_{min}	64 ± 1.7	65 ± 1.7	67 ± 1.7	66 ± 1.7	69 ± 1.5	63 ± 1.8	6.57	<0.001
Heart rate (beats/min)	E_{max}	75 ± 2.7	76 ± 2.8	79 ± 2.1	83 ± 3.3	86 ± 3.9	77 ± 3.3	9.59	<0.001
Body temperature (°C)	E_{max}	37.3 ± 0.1	37.3 ± 0.07	37.4 ± 0.08	37.5 ± 0.09	37.5 ± 0.1	37.3 ± 0.09	2.17	NS
List of Complaints (LC score)									
Acute adverse effects	0-12 h	1.6 ± 0.8	4.0 ± 1.0	6.1 ± 1.4	12 ± 2.5	13.5 ± 3.3	4.6 ± 1.1	10.8	<0.001
Subacute adverse effects	12-24 h	0.3 ± 0.3	0.8 ± 0.3	2.2 ± 1.6	5.9 ± 2.3	4.5 ± 1.9	4.4 ± 1.9	3.69	<0.01
Adverse Effects	E_{max}	1.7 ± 0.8	4.0 ± 1.0	6.8 ± 1.8	13 ± 2.5	14 ± 3.3	6.2 ± 1.8	11.0	<0.001
BDNF (pg/mL)	C_{max}	2953 ± 484	3800 ± 617	3561 ± 464	3848 ± 723	5685 ± 693	4372 ± 880	2.61	<0.05

	Pla	Pla	Pla	Pla	Pla	25	25	25	25	50	50	50	100	100	200
	-	-	-	-	-	µg	µg	µg	µg	µg	µg	µg	µg	µg	µg
	25	50	100	200	200	µg	50	100	200	µg	100	200	µg	200	200
	µg	µg	µg	µg	µg	µg	µg	µg	µg	µg	µg	µg	µg	µg	µg
					+K										

Adjective Mood Rating Scale (AMRS score)															
Well-being	NS	*	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Anxiety	NS	NS	NS	**	NS	NS	NS	*	NS	NS	*	NS	NS	NS	*
Inactivity	NS	NS	***	***	NS	NS	*	*	NS	NS	NS	NS	NS	NS	NS
Extraversion	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Introversion	NS	*	***	***	NS	*	***	***	NS	NS	NS	NS	NS	**	*
Emotional excitation	NS	NS	***	***	NS	NS	***	**	NS	**	*	NS	NS	**	**
Autonomic effects															
Systolic blood pressure (mmHg)	NS	*	**	*	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
E_{max}	NS	NS	NS	**	NS	NS	NS	NS	NS	NS	NS	**	NS	NS	***
Diastolic blood pressure (mmHg)	NS	NS	*	***	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
E_{max}	NS	NS	NS	**	NS	NS	NS	*	NS	NS	NS	**	NS	*	***
Heart rate (beats/min)	NS	NS	**	***	NS	NS	*	***	NS	NS	**	NS	NS	NS	***
Body temperature (°C)	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
List of Complaints (LC score)															
Acute adverse effects	NS	NS	***	***	NS	NS	**	***	NS	*	**	NS	NS	**	***
Subacute adverse effects	NS	NS	*	NS	NS	NS	*	NS	NS	NS	NS	NS	NS	NS	NS
Adverse Effects	NS	NS	***	***	NS	NS	***	***	NS	*	*	NS	NS	*	**
BDNF (pg/mL)	NS	NS	NS	*	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS

* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$; NS, not significant; E_{max} , maximal effect; ΔE_{max} , maximal difference from baseline; C_{max} , maximal concentration

FIG. 4A

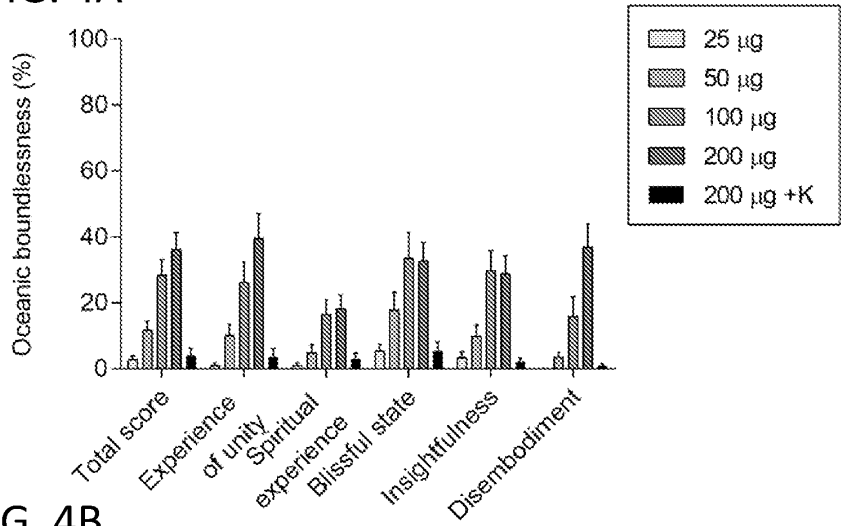


FIG. 4B

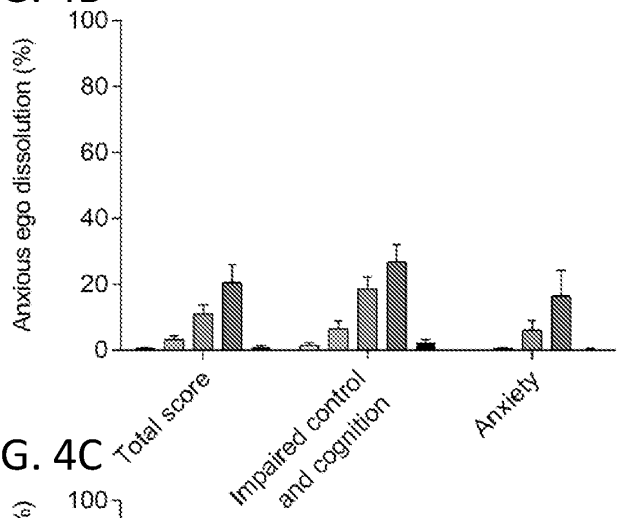


FIG. 4C

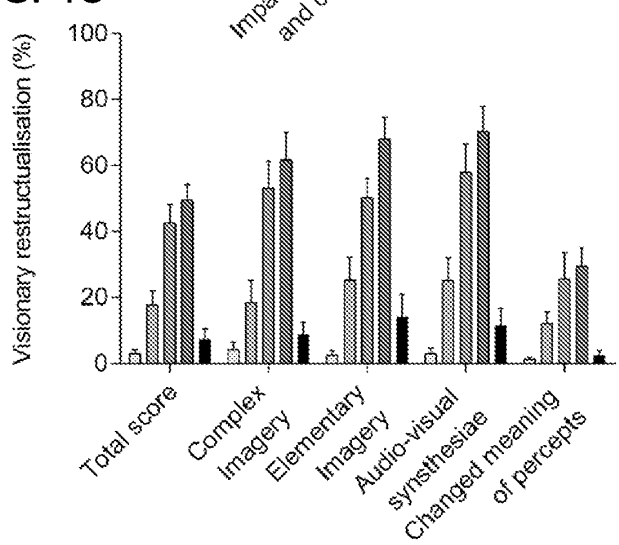


FIG. 5

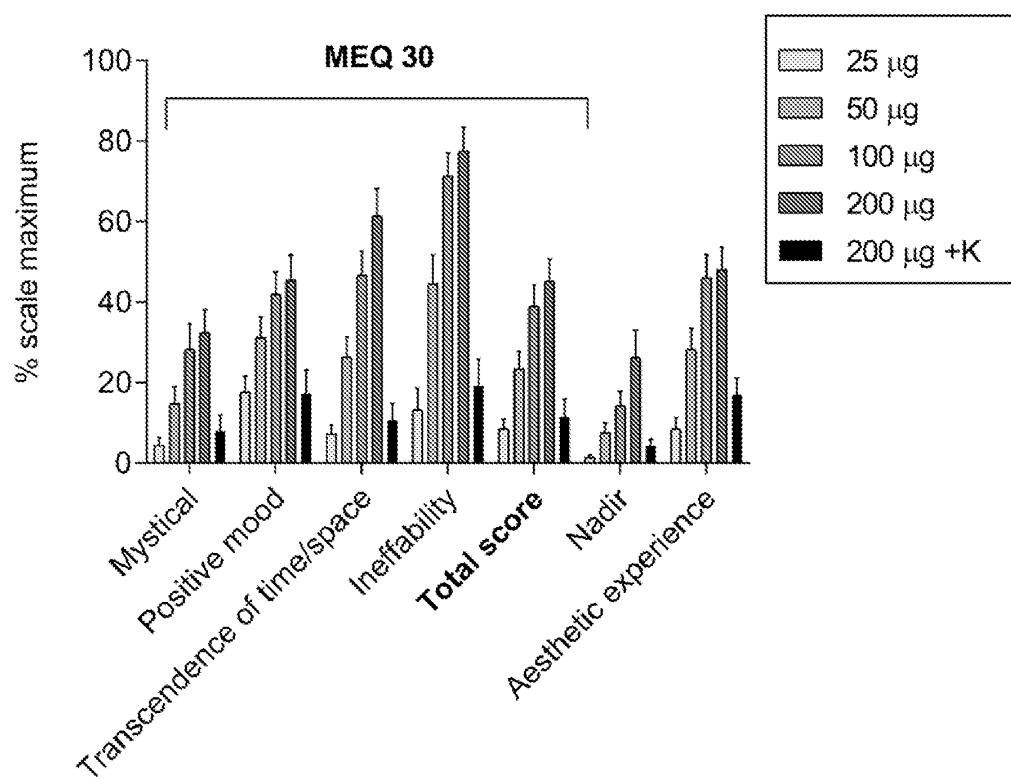


FIG. 6A

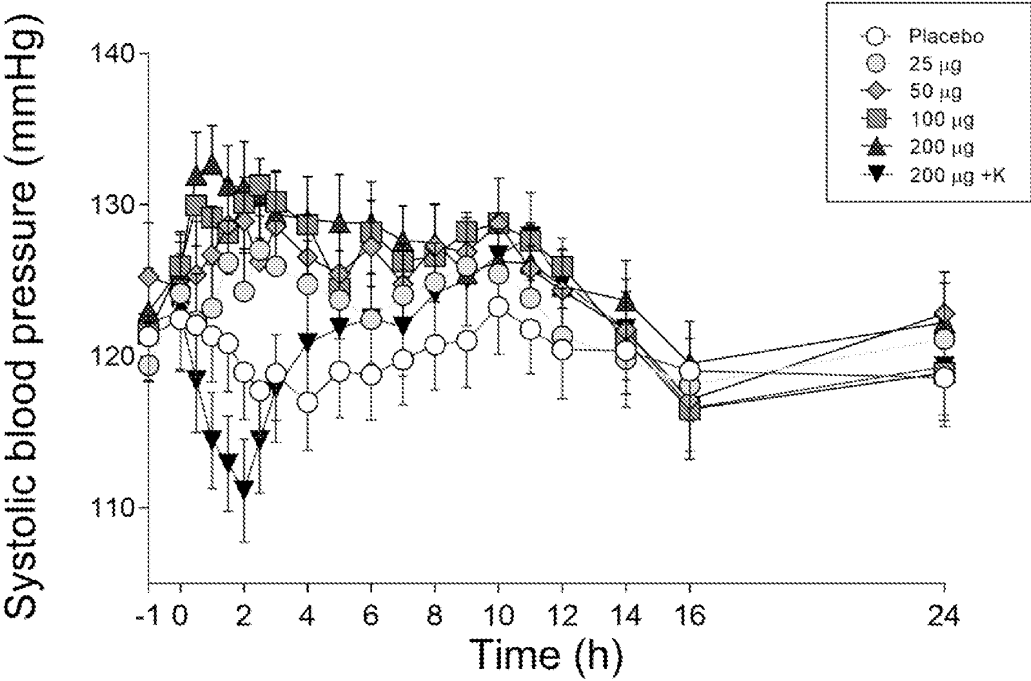


FIG. 6B

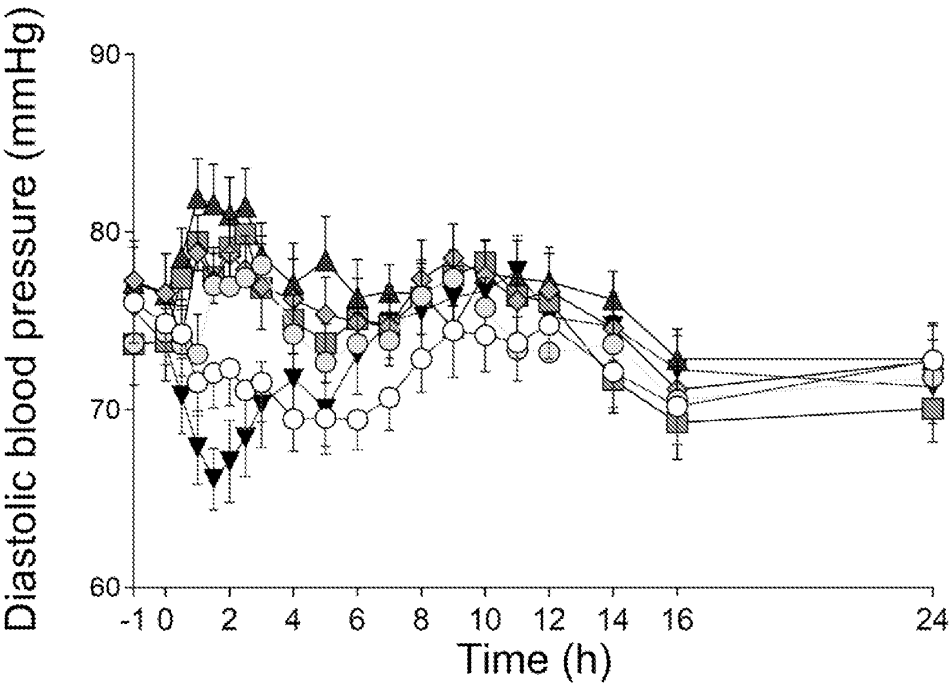


FIG. 6C

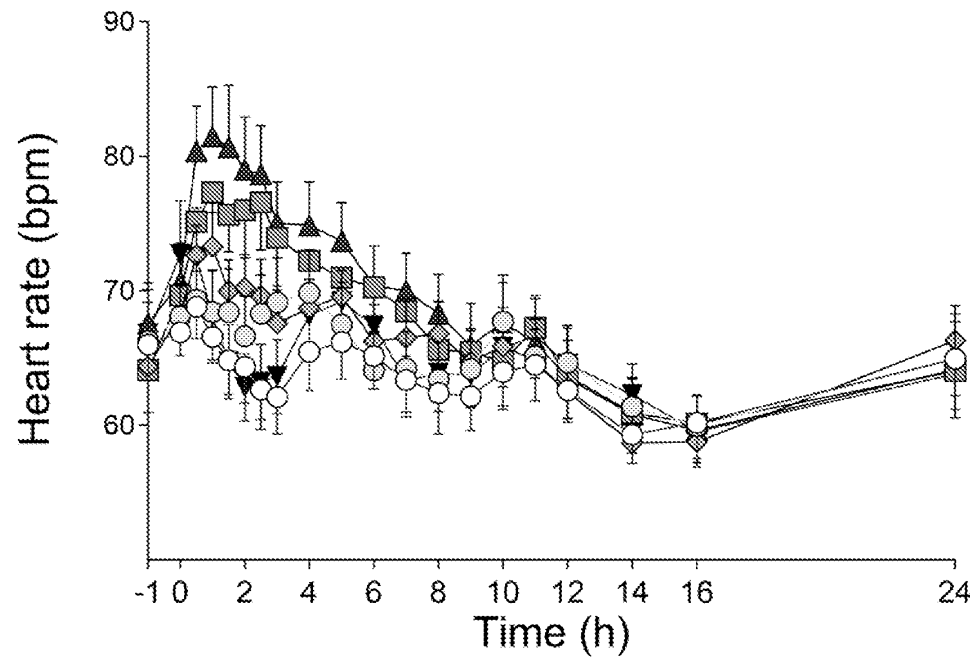


FIG. 6D

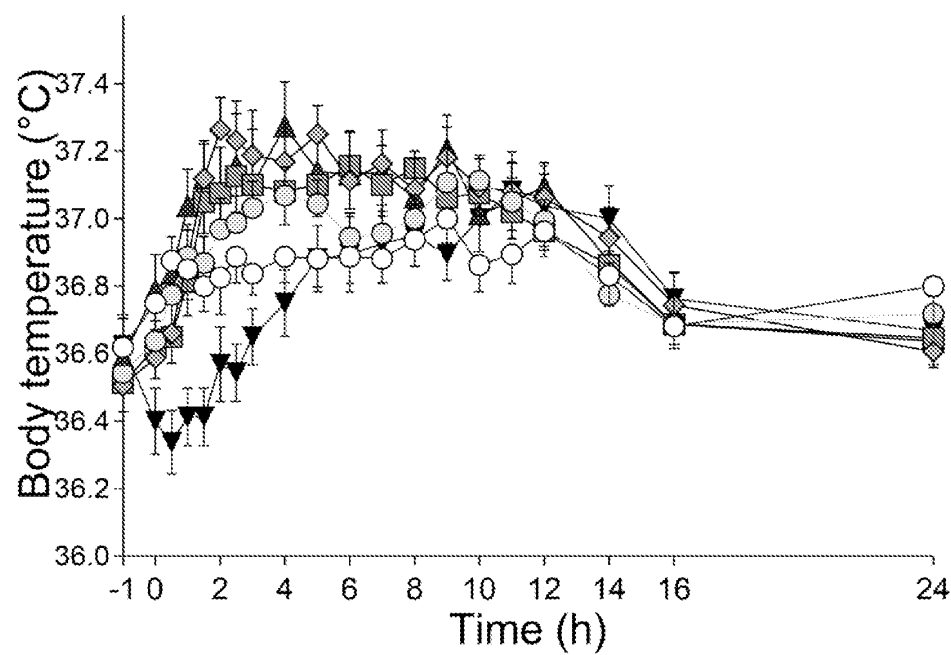


FIG. 7

Acute adverse drug effects

	LSD 25 µg			LSD 50 µg			LSD 100 µg		
	0h	0-12h	12-24h	0h	0-12h	12-24h	0h	0-12h	12-24h
Tiredness	4	4	7	7	6	7	5	7	8
Headache	1	6	4	1	5	4	0	10	9
Lack of concentration	0	7	1	0	6	1	0	11	5
Lack of appetite	0	3	0	0	3	0	0	8	3
Dullness	0	4	1	1	3	2	0	5	4
Brooding	0	2	0	0	3	1	0	7	6
Dry mouth	1	2	2	0	3	3	0	4	2
Feeling of weakness	0	3	0	0	3	2	0	7	3
Uneasiness	0	1	0	1	4	1	0	9	2
Hypersensitivity to certain odours	0	2	0	0	4	2	0	5	2
Lack of energy	1	3	0	0	2	1	0	6	3
Abdominal pain	0	3	0	0	4	1	0	4	1
Obliviousness	0	1	0	0	3	2	0	5	4
Crying tendency	0	1	0	0	1	1	0	5	4
Nausea	0	2	0	0	0	0	0	5	1
Rapid exhaustibility	0	0	0	0	2	1	0	6	2
Dizziness	0	3	0	0	1	1	0	5	2
Excessive urge to urinate	0	2	1	0	2	1	0	3	1
Feel of pressure or fullness	0	0	0	0	3	0	0	3	1
Imbalance	0	1	0	0	0	1	0	7	1
	LSD 200 µg			LSD 200 µg + Ketanserin			Placebo		
Tiredness	4	5	7	6	11	9	5	8	4
Headache	0	5	4	1	5	5	0	3	3
Lack of concentration	0	8	3	1	7	3	0	2	0
Lack of appetite	0	8	1	0	4	2	0	1	0
Dullness	0	4	3	1	2	3	0	1	1
Brooding	1	4	3	0	2	4	0	1	0
Dry mouth	0	4	2	0	3	3	0	3	1
Feeling of weakness	0	5	2	0	2	3	0	0	0
Uneasiness	0	5	2	0	2	4	0	0	0
Hypersensitivity to certain odours	0	6	2	0	3	2	0	1	0
Lack of energy	0	3	2	1	4	3	0	1	0
Abdominal pain	1	3	2	0	3	3	0	2	0
Obliviousness	0	5	2	0	0	2	0	0	0
Crying tendency	0	5	3	0	1	2	0	0	0
Nausea	0	5	3	0	3	1	0	2	1
Rapid exhaustibility	0	5	3	1	1	2	0	0	0
Dizziness	0	3	0	0	4	1	0	0	0
Excessive urge to urinate	0	2	2	0	4	1	0	0	1
Feel of pressure or fullness	0	5	2	0	2	3	0	1	0
Imbalance	0	6	1	0	2	1	0	0	0

Data indicate number of subjects reporting an effect among a total of 16 subjects.

FIG. 8

Pharmacokinetic parameters for different doses
of LSD based on compartmental modeling

Dose (μg)			K ₀₁ (1/h)	λ _z (1/h)	V _z /F (L)	C _{max} (ng/mL)
LSD	25	Geometric mean (95% CI)	2.0 (1.3-3.2)	0.19 (0.16-0.24)	38 (30-47)	0.49 (0.41-0.58)
		Range	0.40-15.1	0.06-0.35	15-102	0.20-0.71
	50	Geometric mean (95% CI)	2.1 (1.5-3.0)	0.19 (0.16-0.23)	35 (31-38)	1.1 (0.99-1.2)
		Range	0.43-19.8	0.06-0.44	22-46	0.68-1.6
	100	Geometric mean (95% CI)	1.8 (1.4-2.4)	0.18 (0.15-0.21)	37 (33-42)	2.0 (1.9-2.2)
		Range	0.7-4.5	0.06-0.24	22-51	1.7-2.9
	200	Geometric mean (95% CI)	1.6 (1.2-2.1)	0.17 (0.14-0.20)	39 (35-43)	3.9 (3.5-4.3)
		Range	0.45-5.03	0.06-0.35	25-67	2.5-6.0
	200 + Ketanserin	Geometric mean (95% CI)	2.3 (1.4-3.8)	0.15 (0.13-0.18)	36 (32-40)	4.4 (4.0-4.8)
		Range	0.6-20.0	0.06-0.24	23-47	3.1-6.8
			t _{max} (h)	t _{1/2} (h)	AUC _∞ (ng·h/mL)	CL/F (L/h)
	25	Geometric mean (95% CI)	1.2 (0.9-1.7)	3.6 (2.9-4.4)	3.5 (2.7-4.5)	7.2 (5.6-9.3)
		Range	0.29-2.7	2.0-12	1.1-12	2.0-22
	50	Geometric mean (95% CI)	1.2 (0.95-1.6)	3.6 (3.0-4.2)	7.4 (6.2-8.9)	6.7 (5.6-8.0)
		Range	0.25-2.5	1.6-11	4.2-25	2.0-11.8
	100	Geometric mean (95% CI)	1.4 (1.2-1.7)	3.9 (3.2-4.7)	15 (12-18)	6.6 (5.4-8.0)
		Range	0.74-2.5	2.9-12	11-47	2.1-9.4
	200	Geometric mean (95% CI)	1.5 (1.3-1.9)	4.1 (3.4-4.9)	31 (25-38)	6.5 (5.3-8.0)
		Range	0.70-5.0	2.0-11	18-127	1.6-11
	200 + Ketanserin	Geometric mean (95% CI)	1.2 (0.85-1.8)	4.5 (3.8-5.3)	36 (30-43)	5.6 (4.6-6.8)
		Range	0.25-4.1	0.25-4.1	25-110	1.8-7.9

AUC_{∞} , area under the plasma concentration-time curve from time zero to infinity; CL/F apparent total clearance; $C_{\max}$, estimated maximum plasma concentration; $t_{1/2}$, estimated plasma elimination half-life; $t_{\max}$, estimated time to reach $C_{\max}$; k_{01} , first-order absorption coefficient; λ_z , first order elimination coefficient; V_z/F volume of distribution.

FIG. 9A

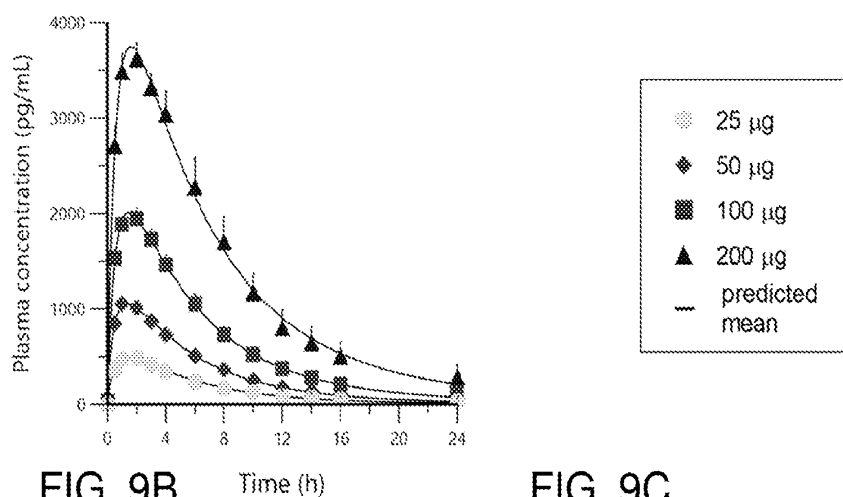


FIG. 9B

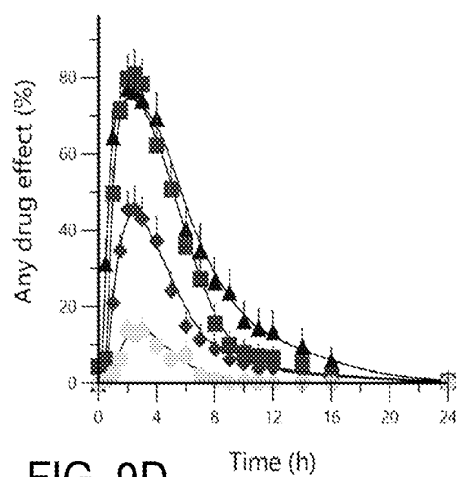


FIG. 9C

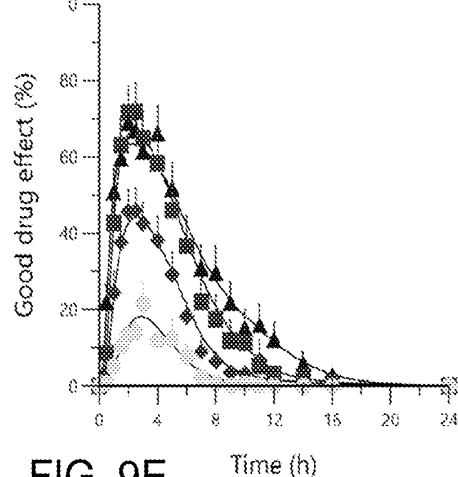


FIG. 9D

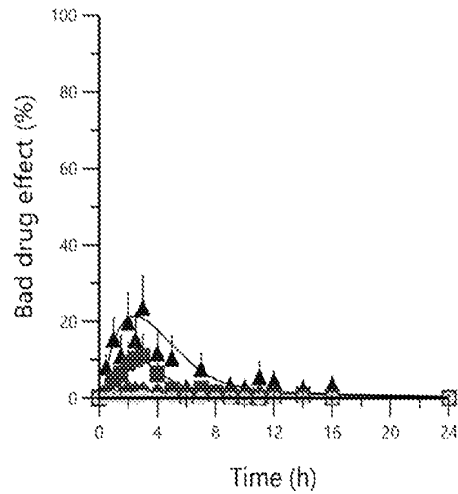


FIG. 9E

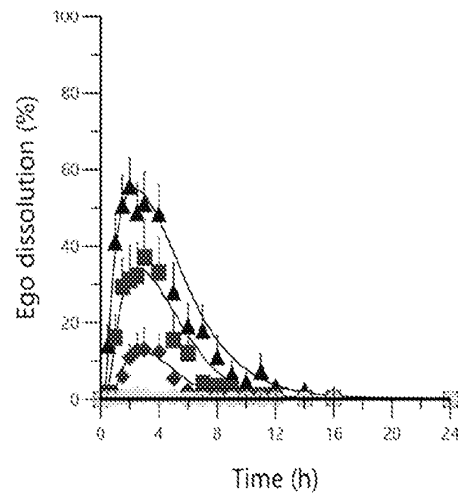


FIG. 10

Characteristics of the subjective response to different doses of LSD

Effect	25 µg	50 µg	100 µg
Time to onset (h)	1.0 ± 0.4 (0.6 - 1.8)	0.7 ± 0.2 (0.4 - 1.2)	0.6 ± 0.2 (0.4 - 0.9)
Time to offset (h)	7.7 ± 2.1 (5.0 - 12.6)	8.1 ± 2.3 (4.9 - 13)	8.9 ± 3.0 (5.8 - 18)
Time to maximal effect (h)	2.8 ± 0.8 (1.8 - 4.9)	2.4 ± 0.6 (1.6 - 3.3)	2.6 ± 1.1 (1.3 - 6.5)
Effect duration (h)	6.7 ± 2.0 (4.3 - 12)	7.4 ± 2.3 (4.4 - 12)	8.3 ± 2.9 (5.0 - 18)
Maximal effect (%)	17 ± 11 (0 - 37)	46 ± 21 (7 - 86)	76 ± 21 (13 - 97)
	200 µg	200 µg + K	
Time to onset (h)	0.4 ± 0.2 (0.1 - 0.9)	not determinable	
Time to offset (h)	11 ± 4.9 (6.3 - 22)	not determinable	
Time to maximal effect (h)	2.2 ± 0.9 (1.3 - 5.1)	not determinable	
Effect duration (h)	11 ± 5.0 (5.6 - 22)	not determinable	
Maximal effect (%)	76 ± 26 (7 - 98)	not determinable	

Parameters are for "any drug effects" as predicted by the PK-PD link model. The threshold to determine times to onset and offset was set individually at 10% of the individual maximal response. Values are mean ± SD (range). Parameters could not be determined for the LSD plus ketanserin treatment condition because the response was too small.

FIG. 11

Pharmacokinetic parameters for different doses of LSD based on non-compartmental analyses

Dose (μg)			Cmax (ng/mL)	tmax (h)	t1/2 (h)	
LSD	25	Geometric mean	0.51	1.2	4.2	
		(95% CI)	(0.43-0.60)	(0.9-1.6)	(3.5-4.9)	
		Range	0.21-0.69	0.4-3	3.2-11	
	50	Geometric mean	1.1	1.2	3.9	
		(95% CI)	(1.0-1.2)	(0.93-1.5)	(3.5-4.5)	
		Range	0.79-1.5	0.50-3.0	3.0-9.7	
	100	Geometric mean	2.0	1.2	4.0	
		(95% CI)	(1.8-2.2)	(0.89-1.7)	(3.5-4.6)	
		Range	1.6-2.9	0.50-3.0	3.2-8.1	
	200	Geometric mean	3.8	1.5	4.2	
		(95% CI)	(3.4-4.3)	(1.1-2.0)	(3.8-4.8)	
		Range	2.4-6.9	0.4-6.0	2.8-9.0	
200 + Ketanserin	Geometric mean	4.3	1.4	4.4		
	(95% CI)	(4.0-4.7)	(0.95-2.1)	(3.7-5.3)		
	Range	3.4-6.3	0.50-4.0	3.1-13		
			AUC24 (ng·h/mL)	AUC∞ (ng·h/mL)	CL/F (L/h)	Vz/F (L)
25	Geometric mean	3.4	3.6	6.8	42	
	(95% CI)	(2.7-4.3)	(2.8-4.7)	(5.3-8.9)	(34-52)	
	Range	1.1-8.9	1.2-12.3	2.0-20	25-143	
50	Geometric mean	7.4	7.7	6.5	37	
	(95% CI)	(6.3-8.6)	(6.4-9.2)	(5.4-7.7)	(33-41)	
	Range	4.3-19	4.4-25	2.0-11	30-51	
100	Geometric mean	15	15	6.5	38	
	(95% CI)	(13-17)	(13-18)	(5.4-7.8)	(33-43)	
	Range	10-35	11-44	2.2-9.3	22-52	
200	Geometric mean	29	31	6.5	40	
	(95% CI)	(24-35)	(25-38)	(5.2-8.0)	(36-45)	
	Range	18-97	18-132	1.5-11	20-60	
200 + Ketanserin	Geometric mean	34	35	5.6	36	
	(95% CI)	(28-40)	(29-44)	(4.6-6.8)	(32-40)	
	Range	25-81	26-12	1.7-7.8	23-50	

AUC, area under the plasma concentration-time curve; AUC_∞, AUC from time zero to infinity; AUC₂₄, from time 0-24; CL/F apparent total clearance; C_{max}, maximum observed plasma concentration; T_{1/2}, plasma half-life; T_{max}, time to reach C_{max}; 95%CI, 95% confidence interval; V_z/F, apparent volume of distribution

FIG. 12

Pharmacokinetic parameters for different doses of O-H-LSD based on non-compartmental analyses

LSD			Cmax (ng/mL)	tmax (h)	t1/2 (h)
Dose (µg)					
O-H-LSD	25	Geometric mean (95% CI)	0.03 (0.02-0.04)	5.0 (4.0-6.1)	8.6 (7.2-10)
		Range	0.01-0.05	2.0-10	5.2-21
	50	Geometric mean (95% CI)	0.07 (0.06-0.07)	4.8 (4.0-5.7)	8.5 (7.4-9.8)
		Range	0.04-0.12	2.0-10	5.7-23
	100	Geometric mean (95% CI)	0.12 (0.10-0.14)	5.0 (4.1-6.1)	8.3 (7.1-9.6)
		Range	0.06-0.18	3.0-10	5.8-18
	200	Geometric mean (95% CI)	0.25 (0.21-0.28)	5.1 (4.4-5.9)	8.2 (6.9-9.8)
		Range	0.15-0.39	3.9-10	5.5-27
	200 + Ketanserin	Geometric mean (95% CI)	0.24 (0.20-0.29)	4.9 (4.4-5.5)	8.6 (7.2-10)
		Range	0.15-0.38	4.0-6.0	6.0-22
			AUC24 (ng·h/mL)	AUC∞ (ng·h/mL)	
	25	Geometric mean (95% CI)	0.39 (0.31-0.47)	0.48 (0.39-0.59)	
		Range	0.16-0.71	0.19-0.89	
	50	Geometric mean (95% CI)	0.82 (0.72-0.92)	1.0 (0.9-1.2)	
		Range	0.51-1.3	0.7-1.7	
	100	Geometric mean (95% CI)	1.6 (1.4-1.8)	1.9 (1.7-2.2)	
		Range	1.1-2.3	1.2-3.3	
	200	Geometric mean (95% CI)	3.3 (2.9-3.7)	4.0 (3.5-4.7)	
		Range	2.1-5.4	2.6-7.1	
	200 + Ketanserin	Geometric mean (95% CI)	3.2 (2.8-3.7)	4.0 (3.5-4.6)	
		Range	2.0-5.0	2.4-5.9	

AUC, area under the plasma concentration-time curve; AUC_∞, AUC from time zero to infinity; AUC₂₄, from time 0-24; CL/F, apparent total clearance; C_{max}, maximum observed plasma concentration; T_{1/2}, plasma half-life; T_{max}, time to reach C_{max}; 95%CI, 95% confidence interval; Vz/F, apparent volume of distribution

FIG. 13

Pharmacodynamic parameter estimates for the LSD effect (PK-PD link model)

Effect	Dose (μ g)	EC ₅₀ (ng/ml)	E _{max} (%)	γ	k _{eo} (1/h)
any drug effect	25	0.77 $\pm$ 0.5	70 $\pm$ 36	4.2 $\pm$ 1.0	1.3 $\pm$ 1.1
	50	0.88 $\pm$ 0.3	81 $\pm$ 30	4.1 $\pm$ 1.3	1.9 $\pm$ 1.5
	100	1.1 $\pm$ 0.3	90 $\pm$ 23	4.7 $\pm$ 0.7	2.1 $\pm$ 1.4
	200	2.0 $\pm$ 0.9	83 $\pm$ 28	5.3 $\pm$ 3.0	4.5 $\pm$ 3.1
good drug effect	25	1.1 $\pm$ 0.6	60 $\pm$ 42	4.5 $\pm$ 0.6	1.6 $\pm$ 1.1
	50	0.93 $\pm$ 0.4	80 $\pm$ 29	4.1 $\pm$ 1.3	1.9 $\pm$ 1.5
	100	1.2 $\pm$ 0.4	83 $\pm$ 30	4.5 $\pm$ 0.9	1.9 $\pm$ 1.0
	200	2.0 $\pm$ 1.2	75 $\pm$ 30	4.1 $\pm$ 1.2	3.1 $\pm$ 1.7
bad drug effect	25	2.1 $\pm$ 0.5	6.3 $\pm$ 15	4.7 $\pm$ 0.4	2.1 $\pm$ 0.9
	50	1.9 $\pm$ 0.6	8.0 $\pm$ 16	4.0 $\pm$ 1.6	2.5 $\pm$ 1.4
	100	2.0 $\pm$ 1.0	20 $\pm$ 34	3.1 $\pm$ 1.3	3.1 $\pm$ 1.5
	200	2.7 $\pm$ 1.2	41 $\pm$ 43	4.0 $\pm$ 1.4	3.4 $\pm$ 1.6
ego dissolution	25	2.1 $\pm$ 0.4	9.8 $\pm$ 22	4.6 $\pm$ 0.5	1.8 $\pm$ 0.5
	50	1.6 $\pm$ 0.7	45 $\pm$ 45	4.7 $\pm$ 0.6	1.8 $\pm$ 1.0
	100	1.8 $\pm$ 0.5	69 $\pm$ 39	4.2 $\pm$ 1.2	2.5 $\pm$ 1.7
	200	2.5 $\pm$ 1.2	77 $\pm$ 30	4.3 $\pm$ 0.9	3.0 $\pm$ 1.7

E_{max}, maximal effect predicted by the PK-PD link model; EC₅₀, predicted drug concentration at effect site producing a half-maximal effect; γ , sigmoid shape parameter; k_{eo}, first-order rate constant for the equilibration process between plasma concentration and effect site (PK-PD model link parameter); values are means $\pm$ standard deviations.

FIG. 14

Drug dose identification after each session and after the study

	LSD 200 µg		LSD 100 µg		LSD 50 µg	
	after Session	after Study	after Session	after Study	after Session	after Study
correctly identified	56%	63%	44%	69%	50%	63%
misclassified as LSD 200 µg			44%	19%	0%	6%
misclassified as LSD 100 µg	38%	31%			25%	0%
misclassified as LSD 50 µg	0%	6%	13%	6%		
misclassified as LSD 25 µg	6%	0%	0%	6%	19%	6%
misclassified as LSD 200 µg + ketanserin	0%	0%	0%	0%	6%	13%
misclassified as placebo	0%	0%	0%	0%	0%	13%
	LSD 25 µg		LSD 200 µg + Ketanserin		Placebo	
	after Session	after Study	after Session	after Study	after Session	after Study
correctly identified	56%	63%	56%	75%	81%	69%
misclassified as LSD 200 µg	0%	0%	0%	0%	0%	6%
misclassified as LSD 100 µg	0%	0%	0%	0%	0%	6%
misclassified as LSD 50 µg	31%	13%	19%	6%	0%	6%
misclassified as LSD 25 µg			19%	13%	13%	13%
misclassified as LSD 200 µg + ketanserin	6%	6%			6%	0%
misclassified as placebo	6%	13%	6%	6%		

FIG. 15

