Overcoming treatment-resistance in chronic depression: A pilot study on outcome and feasibility of the Cognitive Behavioral Analysis System of Psychotherapy as an inpatient treatment program

Eva-Lotta Brakemeier, Martina Radtke, Vera Engel, Johannes Zimmermann, Brunna Tuschen-Caffier, Martin Hautzinger, Elisabeth Schramm, Mathias Berger, Claus Normann

Online Supplementary Material A

A1 Detailed description and explanation of the CBASP inpatient concept

The CBASP inpatient treatment based on the CBASP concept by McCullough [2,A1] was established in 2008 and has been manualized [11]. The CBASP inpatient program includes the following CBASP specific therapy components: individual therapy (two sessions of 50 minutes/week), group psychotherapy (two sessions of 90 minutes/week), physiotherapy with Kiesler Circle Training (one session of 60 minutes/week), occupational group (two sessions of 90 minutes/week), nurse-patient encounters (at least one session of 30 minutes/week), and social worker contact (at least one session of 30 minutes/week).

In the CBASP introduction phase, significant other history and transference hypotheses are compiled in four individual sessions and discussed in the CBASP team meeting. The patient's significant others denote the significant persons who have left their positive or negative "stamps" on the individual shaping how he or she behaves and determining what he or she has come to expect in interpersonal relationships. The transference hypothesis, developed in collaboration with

the patient, is a predictive hypothesis about what the patient is likely to expect from the therapist and how the patient is likely to behave interpersonally in treatment. As a modification to the outpatient treatment, transference hypotheses are not only formulated for the individual therapist but also for the treatment ward team and for the patient group.

In the CBASP main phase, the patient starts with the three CBASP group therapies, in addition to ongoing individual psychotherapy sessions, nurse encounters, and social worker contacts. This phase focuses on the intensified use of the Kiesler circle and on conducting situational analyses with subsequent role-playing events to modify inappropriate behavior. By operating with the Kiesler circle the patients get a deeper understanding of their stimulus character and its impact on others. The situational analysis is the major strategy of CBASP which aims to teach patients' skills to focus on attainable desired outcomes and to use adequate interpretations and behavior to reach them. The situational analysis helps patients to address their problematical situations in behavioral ways. It is also designed to demonstrate patients the link between their own behavior and the interpersonal consequences, since the consequences they report are, for the most part, self-produced. Moreover, CBASP uses the relationship with the therapist and other team members as a tool to help patients to become more aware of their impact on others and to distinguish between adaptive and maladaptive interpersonal relationships. Thus, interpersonal hotspot situations were utilized to offer interpersonal healing experiences by using the disciplined personal involvement with interpersonal discrimination exercises. The aims of these strategies are to modify pathological behavior, to connect patients with their interpersonal environment, and to break the cycle of preoperational functioning [2,11,A1].

In the final phase, i.e., the last two weeks of the inpatient treatment, arrangements are made for hospital discharge and for the continuation of the therapy in the outpatient setting. If patients continue applying the

learned CBASP strategies and want another opportunity for treatment in the inpatient CBASP concept, they can attend a CBASP refresher course lasting four weeks at least six months after their first discharge. In addition, in some cities, CBASP patient support groups have been established to avoid relapse after discharge [11].

The entire CBASP treatment team involved in this study was trained in CBASP by ELB and ES (both certified CBASP trainer). The team consisted of two physicians, two clinical psychologists, nine nurses, and four additional therapists (two art therapists, one physiotherapist, and one social worker). All individual CBASP therapists (five clinical psychologists and three psychiatric residents during the study period) had completed or were in an advanced stage of their psychotherapy training.

For the team, the following CBASP components have been established: team meeting (90 minutes/week), individual supervision for the therapists (60 minutes/week), team supervision (120 minutes/month), and ongoing trainings for the staff (240 minutes/every second month).

A2 Additional information concerning feasibility and acceptance

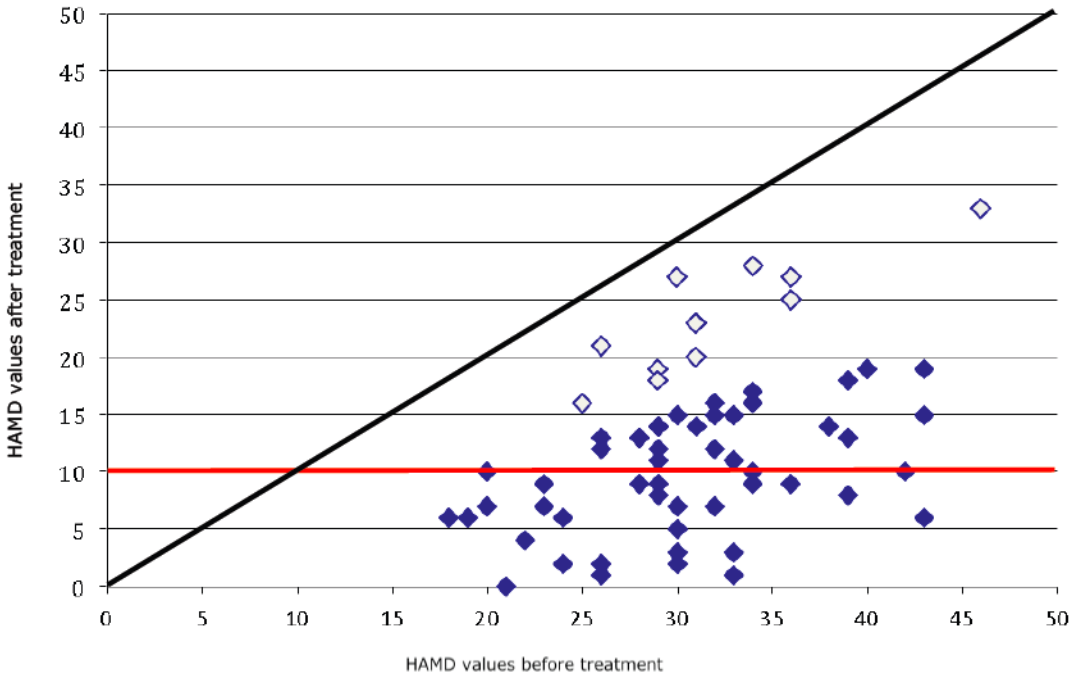
To summarize the acceptance questionnaires, the following percentage of completer patients (N=65) rated the CBASP components as ‘helpful’ or ‘very helpful’: 92.9% physiotherapy with Kiesler Circle Training, 91.2% individual therapy, 87.7% group psychotherapy, 86.2% nurse-patient encounters, 73.9% social worker contact, and 64.7% occupational group. In total, 90.4% judged the overall concept as ‘helpful’ or ‘very helpful’. Concerning CBASP strategies, the therapeutic relationship and the resulting interpersonal experiences were judged as most helpful regarding the individual therapy. The use of the Kiesler circle and the situational analyses were perceived as the most helpful group strategies.

The acceptance of and satisfaction with the CBASP concept by the treatment team was high [A2], and there were no persistent difficulties integrating the concept into the clinical routine.

A3 Additional information concerning the depressive symptomatology and outcome-rates

Figure A1 illustrates the treatment response for each patient of the completer sample, demonstrating that no patient deteriorated.

Figure A1. Treatment results of the inpatient CBASP program in the completer sample (N=65).



Note. Scatter plot of the individual $HAMD_{24}$ (Hamilton Rating Scale for Depression, 24 items, scale 0-75 [16]) scores before and after treatment. All cases below the black diagonal line improved. The unfilled cases are the non-responders (note: two cases 31/23); the filled cases above the red line are the responders; the filled cases below the red line responded and also remitted. Non-responder = not fulfilling criteria for response; responder = fulfilling criterion for response: decrease in symptom severity of at least 50% on the $HAMD_{24}$ from pre to post treatment; remitter = fulfilling criteria for

remission: a score of 10 or less on the $HAMD_{24}$ scale in post treatment. Due to these criteria, all remitters were also responders.

The Figure 1 in the manuscript presents the estimated trajectories of change in MADRS [18], IDS-SR [19], $HAMD_{24}$ [16], and BDI-II [17] in the ITT-sample based on linear mixed-effect models. MADRS and IDS-SR scores steadily decreased during treatment. At discharge, MADRS scores were reduced by 16.59 points (SE = 1.18, $p < .001$, d = 1.89) and IDS-SR scores were reduced by 14.16 points (SE = 1.59, $p < .001$, d = 1.02). Moreover, $HAMD_{24}$ scores decreased by 18.30 points by the time of discharge (SE = 1.01, $p < .001$, d = 2.52). This decrease was also relatively stable during follow-up, with 15.08 points at the six-month follow-up (SE = 1.18, $p < .001$, d = 2.08) and with 13.87 points at the 12-month follow-up (SE = 1.18, $p < .001$, d = 1.91). Similarly, BDI-II scores decreased by 14.6 points by the time of discharge (SE = 1.78, $p < .001$, d = 1.15). Again, this decrease was relatively stable during follow-up with 11.16 points at the six-month follow-up (SE = 2.12, $p < .001$, d = 0.88) and with 10.3 points at the 12-month follow-up (SE = 2.13, $p < .001$, d = 0.81).

The Table A1 summarized the observed $HAMD_{24}$ and BDI-II values at pre, post, six-month, and 12-month follow-up measurement points.

Table A1. Descriptive statistics of the $HAMD_{24}$ and BDI-II values at pre, post, 6-months, and 12-months follow-up measurement

	$HAMD_{24}$[1]			BDI-II[2]		
	n	M	SD	N[3]	M	SD
Pre	70	31.07	6.27	64	33.22	9.73
Post	65	12.43	7.25	63	18.83	12.74
6-months	61	15.21	9.40	40	20.68	14.85
12-months	60	16.87	10.36	36	22.31	14.63

Note. [1] Hamilton Rating Scale for Depression, 24 items, scale 0-75 [16]; [2] Beck Depression Scale, version II, scale 0-63 [17]; [3]Since BDI is a self-rating instrument and not all severely depressed patients could be motivated, the number of patients with completed data is lower in the BDI than in the HAMD being an observer rated interview.

A4 Additional information concerning the interpersonal impact messages

In this study, the Impact Message Inventory [IMI-R; 20] based on the interpersonal circle model by Kiesler [A3] was used to assess the impact message of a patient rated by the therapist. Impact messages are defined as experiences of subtle interpersonal pressures in the communication with another person about what he or she wants the other person to do or not to do [A4]. The IMI-R is developed within the interpersonal tradition [A5]. It is assumed that all interpersonal behaviour patterns can be accounted for by a combination of two central descriptive dimensions: agency and communion. Both span a two-dimensional space referred to as the interpersonal circumplex. In the IMI-R, the interpersonal space is subdivided into eight octants representing combinations of agency and communion, such as hostile-submissive or friendly-dominant [A6,A7].

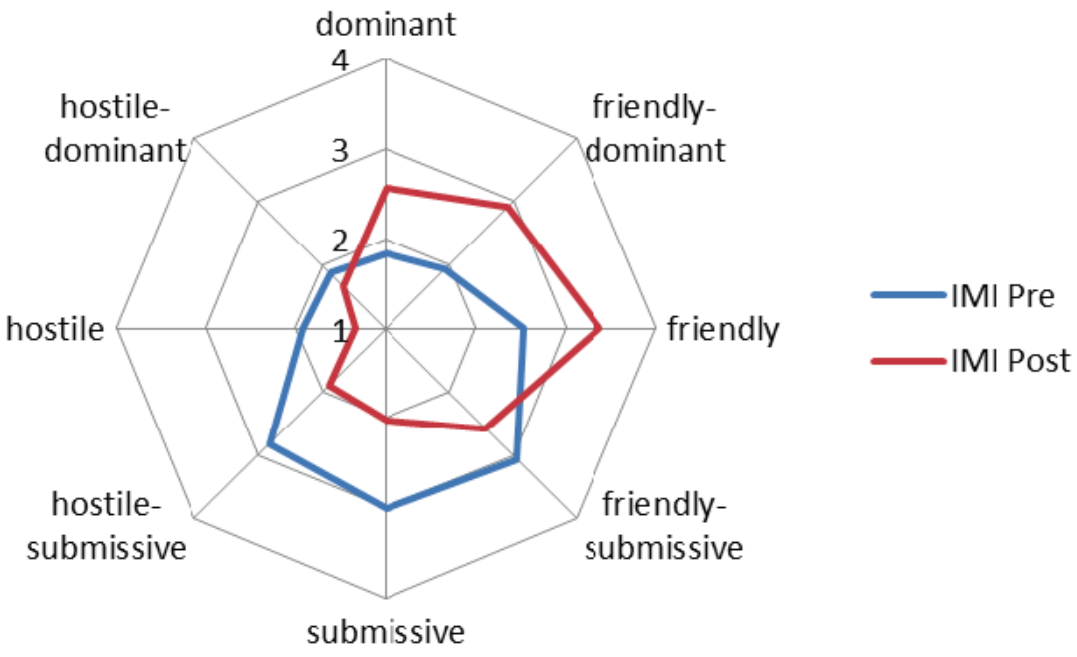
Figure A2 presents the estimated changes in IMI-R ratings in the ITT-sample based on linear mixed-effect models. Patients were perceived by their individual therapists as significantly more dominant (B = 0.73, SE = 0.07, $p < .001$, d = 1.69), friendly-dominant (B = 0.98, SE = 0.08, $p < .001$, d = 1.84), and friendly (B = 0.85, SE = 0.09, $p < .001$, d = 1.69), and as significantly less friendly-submissive (B = -0.49, SE = 0.08, $p < .001$, d = -0.96), submissive (B = -0.98, SE = 0.10, $p < .001$, d = -1.41), hostile-submissive (B = -0.91, SE = 0.10, $p < .001$, d = -1.47), hostile (B = -0.59, SE = 0.09, $p < .001$, d = -1.34), and hostile-dominant (B = -0.21, SE = 0.08, p = .013, d = -0.42). In short, patients improved considerably in terms of dominance and affiliation.

The significant modification of patients' stimulus character (measured by the IMI-R rated by the therapist) underlines McCullough's view that CBASP is effective in improving interpersonal functioning [2,A1]. Patients improved considerably in terms of dominance and affiliation, which might be supported by the integration of the Kiesler circle into the group

therapies. In line, a study with data of the Keller trial [3] found that the CD patients were less hostile and more friendly after therapy [A6].

Of note, the IMI-R was used as a therapeutic instrument in the individual sessions. Thus, the therapists were neither blinded nor objective raters, so there are limitations to the validity of these interpretations. In a future study, the IMI-R should be rated by blinded raters or even by significant others, as in one published trial [A7].

Figure A2. Change in patient stimulus character before and after inpatient treatment



Note. IMI-R (Impact Message Inventory Revised) [20] mean scores of the eight stimulus characteristics of the Kiesler Circle as judged by the individual therapists for their patients before and after treatment.

References Supplementary Material A

A1. McCullough JP: Treating chronic depression with disciplined personal involvement, Cognitive Behavioral Analysis System of Psychotherapy. New York, Springer, 2006.

A2. Brakemeier EL, Engel V, Radtke M, Gumz A, Berger M, Normann C: How did the implementation of a disorder-tailored inpatient CBASP concept for chronically depressed patients influence acceptance, satisfaction, and burnout levels of the treatment team over two years? (in preparation).

A3. Kiesler DJ: The 1982 Interpersonal Circle: A taxonomy for complementarity in human transactions. Psychol Rev 1983;90:185–214.

A4. Pincus AL, Lukowitsky MR, Wright AGC: The interpersonal nexus of personality and psychopathology. In: T Millon, R Kreuger, E Simonsen (Eds.), Contemporary directions in psychopathology: Scientific foundations for DSM-V and ICD-11 (pp. 523–552). New York, Guilford Press, 2010.

A5. Hafkenscheid A: Assessing objective countertransference with a computer-delivered Impact Message Inventory (IMI-C). Clin Psychol Psychother 2012;19(1):37–45.

A6. Constantino MJ, Manber R, Degeorge J, McBridge C, Ravitz P, Zuroff DC, Klein DN, Markowitz JC, Rothbaum BO, Thase ME, Arnow BA: Interpersonal styles of chronically depressed outpatients: Profiles and therapeutic changes. Psychotherapy 2008;45(4):491–506.

A7. Grosse Holtforth M, Altenstein D, Ansell E, Schneider C, Caspar F: Impact messages of depressed outpatients as perceived by their significant others: Profiles, therapeutic change, and relationship to outcome. J Clin Psychol 2011;67(0):1–15.

Overcoming treatment-resistance in chronic depression: A pilot study on outcome and feasibility of the Cognitive Behavioral Analysis System of Psychotherapy as an inpatient treatment program

Eva-Lotta Brakemeier, Martina Radtke, Vera Engel, Johannes Zimmermann, Brunna Tuschen-Caffier, Martin Hautzinger, Elisabeth Schramm, Mathias Berger, Claus Normann

Online Supplementary Material B

Table B1. Add-on Medication of the Intention-to-Treat Sample for each Response Group at Baseline.

Add-on Medication	Remitter (*n* = 28)	Responder (*n* = 25)	Non-Responder (*n* = 12)	Dropout (*n* = 5)	All (*N* = 70)	$p^{\dagger}$
Antidepressants						
Percent receiving no antidepressant	25.0	8.0	25.0	60.0	21.4	
Percent receiving one antidepressant	46.4	60.0	66.7	40.0	54.3	.338
Percent receiving two or more antidepressants	28.6	32.0	8.3	0.0	24.3	

Add-on Medication	Remitter (*n* = 28)	Responder (*n* = 25)	Non-Responder (*n* = 12)	Dropout (*n* = 5)	All (*N* = 70)	***p*†**
Specific received antidepressants						
Selective serotonin reuptake inhibitor (e.g., citalopram, sertraline)	32.1	24.0	41.7	20.0	30.0	.681
5HT/noradrenaline reuptake inhibitor (e.g., venlafaxine, duloxetine)	21.4	52.0	25.0	0.0	31.4	.033*
Noradrenaline/dopamine reuptake inhibitor (e.g., bupropion)	21.4	4.0	0.0	0.0	10.0	.073
Tricyclic antidepressants (e.g., trimipramine)	10.7	20.0	0.0	20.0	12.9	.354
Tetracyclical antidepressants (e.g., mirtazapine)	17.9	24.0	16.7	0.0	18.6	.645
Monoamine oxidase inhibitor (e.g., tranylcypromine)	0.0	4.0	0.0	0.0	1.4	.609
Other antidepressants						
Agomelatine	3.6	0.0	0.0	0.0	1.4	.677

Add-on Medication	Remitter (*n* = 28)	Responder (*n* = 25)	Non-Responder (*n* = 12)	Dropout (*n* = 5)	All (*N* = 70)	*p*†
Antipsychotics						
Percent receiving at least one antipsychotic	28.6	40.0	58.3	20.0	37.1	.135
Specific received antipsychotics						
Atypical antipsychotic	25.0	32.0	58.3	20.0	32.9	.195
Not atypical antipsychotic (low-potency antipsychotic)	7.1	20.0	0.0	20.0	11.4	.237
Mood Stabilizer						
Percent receiving at least one mood stabilizer	7.1	12.0	33.3	20.0	14.3	.223
Specific received mood stabilizer						
Lithium	3.6	8.0	16.7	0.0	7.1	.459
Anticonvulsant (e.g., valproic acid, topiramate, gabapentin, lamotrigine)	7.1	4.0	16.7	20.0	8.6	.462
Anxiolytic and Hypnotic Drugs						
Percent receiving at least one anxiolytic and hypnotic drug	10.7	12.0	0.0	20.0	10.0	.690
Specific received anxiolytic and hypnotic drugs						
Benzodiazepine	10.7	8.0	0.0	0.0	7.1	.599

Add-on Medication	Remitter (*n* = 28)	Responder (*n* = 25)	Non-Responder (*n* = 12)	Dropout (*n* = 5)	All (*N* = 70)	***p*†**
GABAergic Substances (e.g., zolpidem, zopiclone)	3.6	4.0	0.0	20.0	4.3	.310
Stimulants						
Percent receiving at least one stimulant	3.6	4.0	0.0	20.0	4.3	.310
Specific received stimulant						
Methylphenidate	0.0	4.0	0.0	20.0	2.9	.086
Modafinil	3.6	0.0	0.0	0.0	1.4	.677

Note. All values are percentages.

† *p* values are results of chi-square statistics.

Table B2. Add-on Medication of the Intention-to-Treat Sample for each Response Group at Discharge.

Add-on Medication	Remitter (*n* = 28)	Responder (*n* = 25)	Non-Responder (*n* = 12)	Dropout (*n* = 5)	All (*N* = 70)	**p†**
Antidepressants						
Percent receiving no antidepressant	14.3	4.0	16.7	20.0	11.4	
Percent receiving one antidepressant	42.9	56.0	50.0	60.0	50.0	.074
Percent receiving two or more antidepressants	42.9	40.0	33.3	20.0	38.6	
Specific received antidepressants						
Selective serotonin reuptake inhibitor (e.g., citalopram, sertraline)	21.4	8.0	25.0	20.0	17.1	.497
5HT/noradrenaline reuptake inhibitor (e.g., venlafaxine, duloxetine)	17.9	52.0	33.3	0.0	31.4	.022*
Noradrenaline/dopamine reuptake inhibitor (e.g., bupropion)	50.0	40.0	25.0	40.0	41.4	.530
Tricyclic antidepressants (e.g., trimipramine)	28.6	32.0	8.3	20.0	25.7	.454
Tetracyclical antidepressants (e.g., mirtazapine)	10.7	12.0	16.7	0.0	11.4	.803

Add-on Medication	Remitter (*n* = 28)	Responder (*n* = 25)	Non-Responder (*n* = 12)	Dropout (*n* = 5)	All (*N* = 70)	**p**[†]
Other antidepressants						
Agomelatine	0.0	4.0	0.0	20.0	2.9	
Reboxetine	0.0	8.3	0.0	0.0	1.4	.010*
Trazodone	0.0	0.0	16.7	0.0	2.9	
Antipsychotics						
Percent receiving at least one antipsychotic	21.4	44.0	25.0	0.0	28.6	.128
Specific received antipsychotics						
Atypical antipsychotic	14.3	20.0	25.0	0.0	17.1	.602
Not atypical antipsychotic (low-potency antipsychotic)	7.1	24.0	0.0	0.0	11.4	.086
Mood Stabilizer						
Percent receiving at least one mood stabilizer	35.7	24.0	16.7	0.0	25.7	.428
Specific received mood stabilizer						
Lithium	28.6	12.0	8.3	0.0	17.1	.193
Anticonvulsant (e.g., valproic acid, topiramate, gabapentin, lamotrigine)	7.1	16.0	8.3	0.0	10.0	.605

Add-on Medication	Remitter (*n* = 28)	Responder (*n* = 25)	Non-Responder (*n* = 12)	Dropout (*n* = 5)	All (*N* = 70)	**p**[†]
Anxiolytic and Hypnotic Drugs						
Percent receiving at least one anxiolytic and hypnotic drug	0.0	0.0	0.0	40.0	2.8	< .001*
Specific received anxiolytic and hypnotic drugs						
Benzodiazepine	0.0	0.0	0.0	40.0	2.9	< .001*
GABAergic Substances (e.g., zolpidem, zopiclone)	0.0	0.0	0.0	20.0	1.4	.004*
Stimulants						
Percent receiving at least one stimulant	28.6	28.0	41.7	20.0	30.0	.779
Specific received stimulant						
Methylphenidate	7.1	16.0	16.7	20.0	12.9	.701
Modafinil	21.4	12.0	25.0	0.0	17.1	.497

Note. All values are percentages.

[†] *p* values are results of chi-square statistics.