

**Acceptance and Commitment Therapy-based
Group Therapy for Mental Health After Stroke –
a Pilot Study**

Study Protocol and Statistical Analysis Plan

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Background

Stroke is the most common cause of acquired disability in adulthood (Krishnamurthi et al., 2020). After a stroke, every third survivor develops depression, and every fourth survivor develops an anxiety disorder, significantly affecting rehabilitation and quality of life (Blöchl et al., 2019; Kim et al., 2018; Liu et al., 2023; Rafsten et al., 2018). The most commonly studied psychotherapeutic approach after a stroke is cognitive-behavioral therapy (CBT), but the evidence for this approach's efficacy is heterogeneous (Allida et al., 2023; Gao et al., 2016; Lincoln & Flannaghan, 2003). This may be attributed to inadequate adaptation to language and cognitive impairments and a limited fit of the CBT approach for stroke survivors (Kneebone, 2016; Robinson et al., 2019).

An alternative to CBT is a modern, mindfulness-based development of behavioral therapy: Acceptance and Commitment Therapy (ACT). ACT principles are conveyed through metaphors, visualizations, and behavioral exercises. This approach does not directly aim to reduce psychopathology like depressive symptoms but aims to improve psychological flexibility, which is understood as a central resource of mental health. Pilot studies suggest the effectiveness of ACT in individuals with brain damage (Majumdar & Morris, 2019; Rauwenhoff et al., 2023; Sathananthan et al., 2022).

Group therapies are also suitable after a stroke, as they are both economically feasible and implementable in neurological rehabilitation facilities. Additionally, the diversity of perspectives and social integration can promote mental health (Ladwig et al., 2023; McCracken & Gutiérrez-Martínez, 2011).

The efficacy of ACT group therapy has not been investigated after a stroke up to now, and there is no German-language manual adapted for the treatment of individuals with brain injury. Therefore, this pilot study examines the feasibility, acceptance, and preliminary efficacy of an adapted ACT group therapy manual, developed in the UK and proven efficacious in treating individuals with brain damage (e.g., stroke, traumatic brain injury, and brain tumor surgeries) (Bowers et al., 2021).

The manual was translated into German and adjusted to the needs of stroke survivors, who often have a higher age, more comorbidities, and specific neurological impairments compared to the general group of brain-damaged individuals. To reduce cognitive load and adapt to conventions in the German healthcare system, the session duration is shortened from 165 minutes to 90 minutes. Additionally, the study tests outcome questionnaires translated into German and/or simple language for the first time to adjust them to the participants' cognitive capacity.

Objectives

The study aims to provide answers to the following research questions

1. Is the group therapy program feasible?
2. Is the group therapy program accepted by stroke survivors and therapists?
3. Are there first indications on the efficacy of the group therapy to improve psychopathology and/or ACT-specific outcome measures?

Feasibility is hereby assessed via quantitative and objective indicators in accordance with a previous study investigating the efficacy of ACT in people with acquired brain damage (Sathananthan et al., 2022). These indicators include recruitment rates (≥ 3 participants per group within six months), drop-out rates $\leq 20\%$, group attendance $\geq 80\%$ (out of 8 participants * 8 sessions = 64), homework completion rates $\geq 50\%$ (for each session from participants present in session), completion rates of outcome measures $\geq 80\%$, treatment fidelity $\geq 80\%$ (adherence to objectives and contents listed in the manual). Fidelity ratings are based on video recordings of two randomly selected sessions. A research assistant rates the therapists' behavior according to a checklist developed for that session.

Patients rate therapy acceptance with a validated "group therapy session questionnaire" (GTS-P; Zoubek, 2013), which includes six items for each session assessing for example active involvement and comprehensibility of contents, and two items for the entire group therapy on satisfaction and prospect of success. Therapists rate therapy acceptance with a co-developed questionnaire (GTS-T) including twelve items for each session which assess the same six contents as the patients' questionnaire and additional six items on the therapist's involvement and satisfaction. Therapists also rate acceptance for the entire group therapy for each patient on six items also resembling the six items of the patient session questionnaire (GTS-TP). All items are rated on a five-point Likert scale (0 = not true at all to 4 = absolutely true). Mean ratings in a previous study investigating a group therapy for people with diabetes and depression ranged from 2.26 to 2.86 in the different versions of the questionnaire (Zoubek, 2013). Accordingly, a mean value higher than 2 is considered as adequate therapy acceptance by patients and therapists in this study.

Preliminary efficacy is evaluated both via reducing of psychopathological symptoms and increasing of ACT-specific outcomes. ACT aims to improve psychological flexibility, which itself consists of the six processes present in the moment, acceptance, cognitive defusion, self-as-context, values and committed action (Hayes, 2016). In addition to the overall construct of psychological flexibility, the subconstructs valued living and self-as-context are investigated in this study. Valued living represents the action-focused component of *commitment* in ACT and was also reported to increase in people participating in the original group therapy program (Bowers et al., 2021). Self-as-context represents an ACT-specific conceptualization of the self. Self-concept was repeatedly demonstrated as an important determinant of mental health after brain injury (Ownsworth, 2014), yet self-as-context represents the so far least often investigated subconstruct of psychological flexibility in ACT research (Foote et al., 2023). Hence, we included these processes in this pilot study for the investigation of preliminary efficacy.

Study Design

The study employs a pre-post design without a control group. Consequently, there is no randomization or blinding to conditions. Group therapy is conducted with two groups, each consisting of six individuals. The therapy consists of 8 sessions, each lasting 90 minutes. A 30-minute diagnostic examination with questionnaires, including socio-demographic and health-related data, current psychopathology (depressive symptoms, PHQ-9; Kroenke et al., 2001; psychological burden, DASS-21; Lovibond & Lovibond, 1995; anxiety, GAD-7; Spitzer et al., 2006), and ACT-specific outcomes (valued living, VQ; Smout et al., 2014; psychological flexibility, AAQ-ABI; Sylvester, 2011; self-as-context, SACS; Zettle et al., 2018) takes place just before the first session. AAQ-ABI and SACS were translated into German for the first time according to recommendations using independent forward and backward translations (Wild et al., 2005). The questionnaires PHQ-9, DASS-21, GAD-7, AAQ-ABI, VQ, and SACS were also translated into plain language by a professional translation service ("Office for Easy Language Bethel", Bielefeld). After each session, participants and therapists rate the session using the GTS-P and the GTS-T, respectively. After the last session, all participants answer the same questionnaires as before the first session. They evaluate the entire therapy in the GTS-P and indicate if they would recommend the therapy to a friend with similar complaints (yes/no). The pre- and post-assessments are conducted by a trained assistant to exclude biases from the study therapists as facilitators. After the last session, therapists rate the entire therapy for each patient using the GTS-TP.

In a session form, therapists also record the participation of individual persons (Yes/No) and the completion of homework assignments (Yes/No/Incomplete) for each session. If not completed or incomplete, subjective obstacles are queried and documented. This serves to examine feasibility regarding session adherence and homework completion (objective 1).

Selection and Exclusion of Subjects

The participants are recruited through initial consultations at the university's neuropsychological outpatient clinic as well as through self-help groups and practitioners in the region involved in the aftercare of stroke survivors. For this purpose, information flyers are sent to neurological rehabilitation clinics as well as neurological, physiotherapy, occupational therapy, and speech therapy practices. Information and contact details for the study are also published on the homepage of the outpatient clinic and the research unit. Eligibility is evaluated by the principal investigator in an a-priori screening session using relative's information as additional source, if possible.

The study includes N = 12 adult individuals who:

1. have experienced a stroke (ischemic infarction or intracerebral hemorrhage);
2. report increased distress according to the DASS-21;
3. demonstrate sufficient cognitive and linguistic abilities; and
4. show sufficient motivation for therapy.

Increased distress according to the DASS-21 is defined as exceeding a cutoff on at least one of the three subscales of the questionnaire (Depression = D > 10, Anxiety = A > 6, and Stress = S > 10; Nilges & Essau, 2015). In the initial consultation, the cognitive and linguistic performance is assessed based on the participants' self-report and, if applicable, that of a family member, supplemented by the external judgment of the study leader, who has extensive experience in clinical work with individuals with brain damage. If the participant, possibly with input from a family member, and the study leader agree that the person can effectively participate in and benefit from 90-minute group therapy sessions on a weekly basis, the criterion is considered fulfilled. Finally, therapy motivation is assessed by participants assuring their willingness to change their approach to the illness, attend sessions regularly, and complete homework assignments within the therapy program as fully as possible.

Exclusion criteria are assessed based on self-report and external reports by the interested individual, the study leader, and possibly a family member, and include:

1. Interaction or behavioral disorders that significantly hinder group participation (e.g., significantly increased irritability or apathy);
2. Other severe psychiatric disorders (dementia, psychosis, personality disorder, intellectual disability); and
3. Simultaneous psychotherapeutic or neuropsychological treatment.

Treatment of Subjects

Two study therapists lead a group, and the principal investigator serves as a therapist in both groups. The co-therapists are licensed psychotherapists. Table 1 provides an overview of the contents of the sessions and homework.

Table 1. Overview of Sessions and Homework

No.	Content	Homework
1	Introduction, Group Rules, Identification of Complaints, Formulation of Therapy Expectations, Exercise "What is in my Power?" (Derivation of ACT Therapy Rational)	Deepening Therapy Rational: Recognizing uncontrollable things in daily life, associated control strategies, and alternative coping methods
2	Introduction to Mindfulness, Connection with Therapy Rational, Body Scan Exercise with Reflection	Daily Body Scan Exercise, One-time "Mindful Meal" Exercise
3	Discussing the Function of Negative Emotions, Identifying Personal Negative Emotions and	Daily Body Scan Exercise, One-time "Mindful Daily Activity" Exercise

No.	Content	Homework
	Cognitions, Mindful Management of Unhelpful Experiences	
4	Identifying Individual Complaints and Control Strategies as a Review, Exercise "ACT-in-a-Nutshell"	Daily Body Scan Exercise, One-time "Mindful Daily Activity" Exercise, Recording Activities Possible After Stroke
5	Exercise "Mindfulness of Breath," Exercise "Passengers on the Bus" (Cognitive Defusion, Values Orientation), Introduction of Values and Identification of Personal Values with List, Formulation of Initial Approach Steps	Twice daily "Mindfulness of Breath" Exercise, One-time "Mindfulness for Sounds" Exercise, Naming Important Values and Initial Commitments
6	Development of Value-Concordant SMART Goals (Immediate, Short-term, Long-term)	Twice daily "Mindfulness of Breath" Exercise, Completing the Worksheet on Values and Goals
7	Reflection on Values and Goals, Identification of Cognitive Obstacles and Helpful Cognitions in Goal Achievement (Value-Based Life Planning)	Optionally daily Body Scan Exercise or twice daily "Mindfulness of Breath" Exercise
8	Reflection on Value-Based Life Planning and all Sessions, Exercise "Something Positive About..." Conclusion	Guidance on Implementing Value-Based Life Plan and Incorporating Mindfulness into Daily Life

Assessment of Efficacy

Study design, sample size, and application of novel questionnaire versions do not allow to sufficiently prove efficacy of the treatment. However, first indicators of efficacy are investigated by pre-/post comparisons of psychological flexibility (AAQ-ABI) and psychological burden (DASS-21). As secondary outcomes, changes in valued living (VQ), self-as-context (SACS), depressive symptoms (PHQ-9), and anxiety symptoms (GAD-7) are examined. Statistically significant changes are considered indicators of efficacy. In addition, number of participants under the cut-offs on DASS-21 ($D \leq 10$, $A \leq 6$, $S \leq 10$), PHQ-9 (≤ 11), and GAD-7 (≤ 11) before and after the therapy are assessed.

Assessment of Safety and Adverse Events

In the screening session, presence of dysphagia is assessed via self-report to consider and adjust provision of drinks and/or snacks during the group therapy for individuals with impaired swallowing functions. Regarding all other physical health risks, legal and university internal protective measures are followed.

Severe adverse events (SAEs) are recorded after half of the sessions (end of session 4) and after the last session. SAEs include unplanned admissions to psychiatric ward, severe self-mutilating behavior with threat to life, suicide attempts, and death. There is also space on the questionnaire to report further burdensome events. If participants miss a session without giving notice, therapists contact them or relatives via telephone to exclude SAEs. After reporting a SAE, a study therapist immediately counsels the participant on treatment options. In case of death, relatives are offered counseling. Reporting of an SAE leads to immediate pausing of the study. Each SAE is then reported to two psychotherapists who do not participate in facilitating the study therapy. They assess whether a causal relationship between the SAE and the intervention is probable. If a probable relationship is determined, the study is immediately terminated.

Adverse events (AEs) are defined as an increase in documented symptoms of depression, anxiety, and stress, or the emergence of new symptoms by the end of therapy. Participants experiencing new symptoms are offered counseling on further treatment options. During the group therapy, participants may always approach therapists to report increased burden. Therapists may also decide to address suspected increase of burden in individual participants. In case of increased burden, participants are offered counselling on treatment options.

Statistical Analysis Plan

Missing values are replaced by multiple imputation including all assessed variables. Outliers are identified by visual inspection and inclusion/exclusion is decided on a case-by-case approach. Estimates are calculated based on 95% confidence intervals.

Feasibility (research question 1) is assessed by frequencies fulfilling the predefined cut-offs (see objectives).

The acceptance score of > 2 is evaluated by Wilcoxon-tests for one sample (one-sided) for all versions of the GTS (-P mean of single sessions and entire therapy, -T, and -TP). Significant changes in primary outcomes psychological flexibility (AAQ-ABI) and psychological burden (DASS-21) are assessed with Wilcoxon-tests for paired samples (one-sided); p -value is Bonferroni-adjusted ($p = .025$). Significant changes in secondary outcomes valued living (VQ), self-as-context (SACS), depressive symptoms (PHQ-9), and anxiety symptoms (GAD-7) are assessed with Wilcoxon-tests for paired samples (one-sided); p -value is Bonferroni-adjusted ($p = .0125$). Individual changes in primary and secondary outcomes are also based on reliable change indices with a significance level of $\alpha = .90$ (one-sided).

Sensitivity analyses examine the influence of the baseline variables age, gender, kind of stroke (ischemia vs. hemorrhage), current use of prescribed psychotropic drugs (yes/no), previous mental disorder (yes/no), and previous use of psychotherapy (yes/no) on changes in primary and secondary outcomes. These bivariate associations are investigated by Pearson correlations (for continuous covariates) and Chi² tests (for categorical covariates; $p = .05$, two-sided) using the difference scores of the outcomes. Likewise, associations between therapy acceptance and the changes in efficacy outcomes (AAQ-ABI, DASS-21, VQ, SACS, PHQ-9 and GAD-7) are exploratively analyzed.

Ethics

All participants give written informed consent. The study was approved by the ethics review board of Bielefeld University (EUB-2023-341).

References

- Allida, S. M., Hsieh, C.-F., Cox, K. L., Patel, K., Rouncefield-Swales, A., Lightbody, C. E., House, A., & Hackett, M. L. (2023). Pharmacological, non-invasive brain stimulation and psychological interventions, and their combination, for treating depression after stroke. *The Cochrane Database of Systematic Reviews*, 7(7), CD003437. <https://doi.org/10.1002/14651858.CD003437.pub5>
- Blöchl, M., Meissner, S., & Nestler, S. (2019). Does depression after stroke negatively influence physical disability? A systematic review and meta-analysis of longitudinal studies. *Journal of Affective Disorders*, 247, 45–56. <https://doi.org/10.1016/j.jad.2018.12.082>
- Bowers, H., Hill, G [Geoffrey], Webster, A., & Bowman, A. R. (2021). Living well with neurological conditions: Clinical outcomes, insights and reflections on three years of Acceptance and Commitment Therapy group intervention. *The Neuropsychologist*, 1(12), 33–42. <https://doi.org/10.53841/bpsneur.2021.1.12.33>
- Foote, H., Bowen, A., Cotterill, S., Hill, G [Geoff], Pieri, M., & Patchwood, E. (2023). A scoping review to identify process and outcome measures used in acceptance and commitment therapy research, with adults with acquired neurological conditions. *Clinical Rehabilitation*, 37(6), 808–835. <https://doi.org/10.1177/02692155221144554>
- Gao, J., Lin, M., Zhao, J., Bi, S., Ni, Z., & Shang, X. (2016). Different interventions for post-ischaemic stroke depression in different time periods: A single-blind randomized controlled trial with stratification by time after stroke. *Clinical Rehabilitation*, 31(1), 71–81. <https://doi.org/10.1177/0269215515626232>
- Hayes, S. C. (2016). *Acceptance and commitment therapy: The process and practice of mindful change* (2. ed.). Guilford Press.
- Kim, E.-S., Kim, J.-W., Kang, H.-J., Bae, K.-Y., Kim, S.-W., Kim, J.-T., Park, M.-S., Cho, K.-H., & Kim, J.-M. (2018). Longitudinal impact of depression on quality of life in stroke patients. *Psychiatry Investigation*, 15(2), 141–146. <https://doi.org/10.30773/pi.2017.10.11>
- Kneebone, I. I. (2016). Stepped psychological care after stroke. *Disability and Rehabilitation*, 38(18), 1836–1843. <https://doi.org/10.3109/09638288.2015.1107764>
- Krishnamurthi, R. V., Ikeda, T., & Feigin, V. L. (2020). Global, regional and country-specific burden of ischaemic stroke, intracerebral haemorrhage and subarachnoid haemorrhage: A systematic analysis of the Global Burden of Disease Study 2017. *Neuroepidemiology*, 54(2), 171–179. <https://doi.org/10.1159/000506396>
- Kroenke, K [K.], Spitzer, R. L [R. L.], & Williams, J. B. (2001). The PHQ-9: Validity of a brief depression severity measure. *Journal of General Internal Medicine*, 16(9), 606–613. <https://doi.org/10.1046/j.1525-1497.2001.016009606.x>
- Ladwig, S., Werheid, K., Südmeyer, M., & Volz, M. (2023). Predictors of post-stroke depression: Validation of established risk factors and introduction of a dynamic perspective in two longitudinal studies. *Frontiers in Psychiatry*, 14. <https://doi.org/10.3389/fpsy.2023.1093918>

- Lincoln, N. B., & Flannaghan, T. (2003). Cognitive behavioral psychotherapy for depression following stroke: A randomized controlled trial. *Stroke*, *34*(1), 111–115.
<https://doi.org/10.1161/01.STR.0000044167.44670.55>
- Liu, L., Xu, M., Marshall, I. J., Da Wolfe, C., Wang, Y., & O'Connell, M. D. L. (2023). Prevalence and natural history of depression after stroke: A systematic review and meta-analysis of observational studies. *PLoS Medicine*, *20*(3), e1004200.
- Lovibond, P. F., & Lovibond, S. H. (1995). The structure of negative emotional states: Comparison of the Depression Anxiety Stress Scales (DASS) with the Beck Depression and Anxiety Inventories. *Behaviour Research and Therapy*, *33*(3), 335–343. [https://doi.org/10.1016/0005-7967\(94\)00075-U](https://doi.org/10.1016/0005-7967(94)00075-U)
- Majumdar, S., & Morris, R. (2019). Brief group-based acceptance and commitment therapy for stroke survivors. *British Journal of Clinical Psychology*, *58*(1), 70–90.
<https://doi.org/10.1111/bjc.12198>
- McCracken, L. M., & Gutiérrez-Martínez, O. (2011). Processes of change in psychological flexibility in an interdisciplinary group-based treatment for chronic pain based on Acceptance and Commitment Therapy. *Behaviour Research and Therapy*, *49*(4), 267–274.
<https://doi.org/10.1016/j.brat.2011.02.004>
- Nilges, P., & Essau, C. (2015). Die Depressions-Angst-Stress-Skalen: Der DASS - ein Screeningverfahren nicht nur für Schmerzpatienten [Depression, anxiety and stress scales : DASS-A screening procedure not only for pain patients] [Depression, anxiety and stress scales: DASS--A screening procedure not only for pain patients]. *Schmerz*, *29*(6), 649–657.
<https://doi.org/10.1007/s00482-015-0019-z>
- Owensworth, T. (2014). *Self-identity after brain injury* (1st ed.). *Neuropsychological rehabilitation: A modular handbook*. Psychology Press.
- Rafsten, L., Danielsson, A., & Sunnerhagen, K. S. (2018). Anxiety after stroke: a systematic review and meta-analysis. *Journal of Rehabilitation Medicine*, *50*(9), 769–778.
- Rauwenhoff, J. C. C., Bol, Y., Peeters, F., van den Hout, A. J. H. C., Geusgens, C. A. V., & van Heugten, C. M. (2023). Acceptance and commitment therapy for individuals with depressive and anxiety symptoms following acquired brain injury: A non-concurrent multiple baseline design across four cases. *Neuropsychological Rehabilitation*, *33*(6), 1018–1048.
<https://doi.org/10.1080/09602011.2022.2053169>
- Robinson, P. L., Russell, A., & Dysch, L. (2019). Third-wave therapies for long-term neurological conditions: A systematic review to evaluate the status and quality of evidence. *Brain Impairment*, *20*(1), 58–80. <https://doi.org/10.1017/BrImp.2019.2>
- Sathanathan, N., Dimech-Betancourt, B., Morris, E., Vicendese, D., Knox, L., Gillanders, D., Das Nair, R., & Wong, D. (2022). A single-case experimental evaluation of a new group-based intervention to enhance adjustment to life with acquired brain injury: Valiant (valued living after neurological trauma). *Neuropsychological Rehabilitation*, *32*(8), 2170–2202.
<https://doi.org/10.1080/09602011.2021.1971094>
- Smout, M., Davies, M., Burns, N., & Christie, A. (2014). Development of the Valuing Questionnaire (VQ). *Journal of Contextual Behavioral Science*, *3*(3), 164–172.
<https://doi.org/10.1016/j.jcbs.2014.06.001>
- Spitzer, R. L [Robert L.], Kroenke, K [Kurt], Williams, J. B. W., & Löwe, B. (2006). A brief measure for assessing generalized anxiety disorder: The GAD-7. *Archives of Internal Medicine*, *166*(10), 1092–1097. <https://doi.org/10.1001/archinte.166.10.1092>
- Sylvester, M. (2011). *Acceptance and Commitment Therapy for improving adaptive functioning in persons with a history of pediatric acquired brain injury* [Doctoral thesis]. University of Nevada, Reno.

- Wild, D., Grove, A., Martin, M., Eremenco, S., McElroy, S., Verjee-Lorenz, A., & Erikson, P. (2005). Principles of good practice for the translation and cultural adaptation process for patient-reported outcomes (PRO) measures: Report of the ISPOR task force for translation and cultural adaptation. *Value in Health, 8*(2), 94–104. <https://doi.org/10.1111/j.1524-4733.2005.04054.x>
- Zettle, R. D., Gird, S. R., Webster, B. K., Carrasquillo-Richardson, N., Swails, J. A., & Burdsal, C. A. (2018). The Self-as-Context Scale: Development and preliminary psychometric properties. *Journal of Contextual Behavioral Science, 10*, 64–74. <https://doi.org/10.1016/j.jcbs.2018.08.010>
- Zoubek, K. (2013). *Prozessevaluation einer kognitiv- verhaltenstherapeutischen Gruppentherapie bei Diabetes und Depression [Process evaluation of a cognitive-behavioral group therapy for diabetes and depression]: Entwicklung und Validierung der Patienten- und Therapeuten-Gruppentherapiestundenbögen (GTS-P, GTS-T, GTS-TP) zur Vorhersage des Therapieerfolgs [Development and validation of the patient and therapist group therapy questionnaires (GTS-P, GTS-T, GTS-TP) for predicting therapy success]* [Doctoral thesis]. Johannes Gutenberg-Universität, Mainz.