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Indicated Stress Prevention Addressing Adolescents with High Stress Levels Based on Principles of Acceptance and Commitment Therapy: A Randomized Controlled Trial

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Abstract
Introduction: Stress affects many adolescents and is associated with physical and mental health symptoms that can have a negative impact on normative development. However, there are very few evidence-based, specific treatment approaches. The aim of the study was to investigate an eight-session group intervention using components of Acceptance and Commitment Therapy (ACT) enriched with elements of CBT (psychoeducation, problem solving) and art therapy, compared to a waitlist control (WLC) group, regarding its efficacy in reducing stress and associated symptoms. ***Methods:*** We conducted a randomized controlled trial in eight cohorts. Eligible participants were 13–18 years old with elevated stress levels. Via block-randomization (n = 70), participants were allocated to receive ACT (n = 38) or WLC (n = 32) and subsequent ACT. We used a multimodal assessment (self-reports, interviews, ecological momentary assessment, physiological markers) before treatment (T1), after the training of the ACT group (T2) and after subsequent training in the WLC group (T3). Primary outcome was perceived stress at T2 assessed with the Perceived Stress Scale. The trial was preregistered at the German Clinical Trials Register (ID: DRKS00012778). ***Results:*** Results showed significantly lower levels of perceived stress in the ACT group at T2, illustrating superiority of ACT compared to WLC with a medium to large effect size (d = 0.77). Furthermore, the training was effective in the reduction of symptoms of school burnout and physical symptoms associated with stress. ***Conclusion:*** Indicated prevention, especially when based on the principles of ACT and CBT, seems efficient in significantly decreasing stress in adolescents with increased stress.

Introduction

The concept of "allostatic load" comprises both stressful life events as well as chronic stress [1] and includes, among others, a biopsychological perspective [2]. "Allostatic overload" occurs when the demands of the environment go beyond a person's ability to cope [3]. In sensitive phases of brain development, increased allostatic

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load can have a long-lasting impact on neuronal networks [3]. In children and adolescents, increased allostatic load is associated with poorer health outcomes [3]. Elevated stress levels in students are associated with emotional and behavioral problems as well as psychosomatic symptoms [4–6]. Stress in adolescents is also an issue of economic relevance associated with elevated healthcare costs [6]. These severe consequences underline the particular importance of stress prevention in this age group.

Studies concerning stress prevention in adult occupational settings show that approaches based on cognitive behavioral therapy (CBT) appear especially effective [7]. Web- and computer-based stress-management interventions show significant effects in the reduction of adult stress, wherein interventions based on CBT have yielded the largest effect sizes [8]. There is also preliminary evidence that ecological momentary interventions [9] and virtual reality-based interventions, based on established approaches such as CBT [10], can help reduce stress. Other approaches may include meditation [11], physical exercise [12], or mindfulness-based interventions [13–15].

Adolescence is a sensitive phase associated with increased vulnerability to stress [16]. In youth, school-related stress, as well as concerns regarding the future, are among the most frequent sources of stress experiences [17]. Female adolescents might be even more affected by stress than males [18, 19]. Researchers have recently coined the term "school burnout," a pattern of symptoms of school-related exhaustion, cynicism, and feelings of inadequacy [20]. Correspondingly, many interventions are conducted in school settings. A recent meta-analysis on school-based prevention in adolescents in the USA [21] found only a small number of studies addressing stress, with no significant effects. A meta-analysis focusing on interventions to address adolescent stress using mindfulness-based interventions in school settings worldwide yielded a small but significant effect, but only when compared to passive control conditions [22]. The differing results of the two reviews might be explained by variations in the study setting: the inclusion criteria regarding the eligible interventions (mindfulness-based vs. all types of interventions), the countries where the primary studies took place, as well as the date of the finalization of the literature search, differed between the two meta-analyses. Further, both reviews only found a few studies with a stress-related outcome. *Universal prevention* approaches address the general population, whereas *targeted* or *indicated prevention* approaches address individuals already showing some symptoms of a disease but not (yet) meeting diagnostic criteria [23]. Targeted prevention approaches have yielded larger effect sizes than universal prevention [21].

One important factor influencing the level of perceived stress is social support. Camara et al. [24] outline the dual role of interpersonal relationships in adolescent stress. On the one hand, interpersonal stressors substantially contribute to experienced distress, and on the other hand, young people name social support as one of the key strategies to combat stress. In the traditional literature on the role of social support in the context of well-being, two hypotheses are discussed: the *direct effect model* (postulating a general positive effect of social support) and the *buffering model* (claiming that social support serves as a protective influence on the impact of stress) [25]. A large meta-analysis provided evidence for both models but also found that some stressful conditions can make it impossible for youth to use the benefits of social support in the sense of reverse stress buffering [26]. The crucial role of social support in the context of perceived stress suggests designing preventive approaches in a group-based context.

In a meta-analysis including both adult and adolescent samples, stress reduction programs based on psychoeducation show small but significant effects [27]. The meta-analysis included three trials with adolescent samples [28–30], using interventions either based on Meichenbaum's stress inoculation training [31] or on the principles of CBT combined with relaxation methods. All included studies yielded significant improvements. In the context of psychoeducation, another trial examined the effectiveness of a school-based indicated prevention program to improve coping in adolescents [32]. At-risk students were identified based on the assessment of depressive symptoms, a problem checklist, and a coping scale. The program yielded significant effects in the reduction of depression scores and improved coping compared to two control groups. However, this study only assessed coping, not stress, neither as a criterion for inclusion in the targeted prevention nor as an outcome.

A meta-analysis on the effectiveness of mindfulness on mental health in children and adolescents shows that this method can reduce stress and is mostly used in non-clinical populations [33]. Another approach that was successfully adapted to adolescents is well-being therapy [34]. Studies show its positive effects in the prevention of psychological distress in adolescents [35, 36].

Earlier research by our group investigating a school-based universal stress-prevention program within a randomized controlled trial (RCT) provided evidence that especially students who are severely affected by stress seem to benefit the most [37], again suggesting that

indicated prevention is warranted in this context. Despite this evidence, to our knowledge, there are hardly any studies using an indicated stress-prevention approach in adolescents. There is a published pilot trial using an indicated approach to reduce stress in $n = 32$ pupils aged 12–18 years [38], illustrating a reduction of perceived stress.

In the last decades, traditional CBT – which shows effectiveness in the prevention of stress in adults – has been enriched by new approaches including Acceptance and Commitment Therapy (ACT [39]). Acceptance-based therapy approaches focus on developing a different way of dealing with thoughts and feelings instead of changing the content of the thoughts or their appearance per se [40]. ACT assumes that the avoidance of disliked emotions, thoughts, or body sensations contributes to the development and maintenance of a wide range of mental disorders [40]. The reduction of psychopathological symptoms is not a primary goal of ACT [41]. Instead, clients are supported in a process which aims to increase psychological flexibility [41]. It is based on six interrelated core processes (acceptance, defusion, values, committed action, contact with the present moment, self as context [42]). The theoretical basis of ACT is the Relational Frame Theory [43], which underscores the immense impact of language on the way we perceive the world. In the context of ACT, this can lead to problems since cognitions which prevent us from aligning our behavior to our values are represented through language.

ACT has been found to be efficacious for a variety of conditions [44], also in adolescents [45]. Since ACT is not designed as a diagnosis-specific approach [46], it appears suited to stress prevention and treatment [47, 48], also in adolescents [49]. A recent systematic review and meta-analysis of our group on ACT for stress in youth [50] identified significant research gaps in existing studies. There are only very few programs using ACT for preventing adolescent stress [38, 51–59]. Most of the published trials are aimed at unspecific target groups using, for example, school-based settings (universal prevention). Besides the disadvantages of a high expense – with a comparably large proportion of participants not affected by stress at all – these studies often lack proper randomization, frequently within quasi-randomized settings, for example, in school classes [51, 52, 57]. Further limitations of existing studies are small sample sizes [38, 55, 60] as well as biases by a lack of blinding between therapeutic and scientific personnel. Even though the conclusions that can be drawn from the current literature are limited, there is preliminary evidence that ACT may constitute an effective approach to reduce stress in the age group of interest. Consequently, a methodologically rigorous trial is urgently needed in the field.

Research conducted using targeted prevention approaches in adolescent stress is scarce. There are some RCTs addressing burdened youth, especially adolescents suffering from chronic physical conditions. Stress-prevention trials were conducted to support adolescents affected by diabetes using, for example, home-based psychotherapy [61], ACT [53], or group-based training in coping skills [62]. Results indicate significant reductions of (illness-related) stress and physical markers of stress. Further, stress prevention was successfully adapted to a sample of youth with neurofibromatosis [63]. A virtual mind-body intervention led to a greater reduction of stress in the experimental group compared to the control group. A resilience training program to support youth with cancer resulted in improved resilience and decreased psychological distress [64]. Other interventions effectively addressing other types of psychological stress factors in youth focus, for example, on pregnant adolescents [65] or sexual or gender minorities [66]. A prevention intervention based on well-being therapy for at-risk adolescents did not improve perceived stress for combined participants, but in female students [67]. However, to our knowledge, to date, there has been no trial with a sufficient sample size using an indicated approach addressing pupils suffering from elevated stress levels.

Here, we conducted a randomized controlled trial (RCT) to investigate the effects of a group intervention based on the principles of ACT on perceived stress in an adolescent sample with elevated stress. The aim of the study was to investigate the effects of a psychologist-led, group-based, targeted stress-prevention training (ACT) compared to a waitlist control (WLC). Our primary hypothesis was that adolescents in the ACT group would report significantly lower levels of perceived stress than those in the WLC group following the intervention.

Materials and Methods

General Procedures

The RCT was conducted at the Department of Child and Adolescent Psychiatry, University Hospital Heidelberg. Approval of the local ethics committee was obtained before recruitment (Study ID: S-014/2017). Prior to first-patient-in, the trial was registered at the German Clinical Trials Register (DRKS; ID: DRKS00012778). We calculated the required sample size in advance based on the theoretical considerations concerning the expected effect size. To estimate the required sample size, we used data from an indicated burnout prevention trial in adults [68]. In this study, burnout was measured with the Maslach Burnout Inventory [69]. Our power analysis was based on the reported

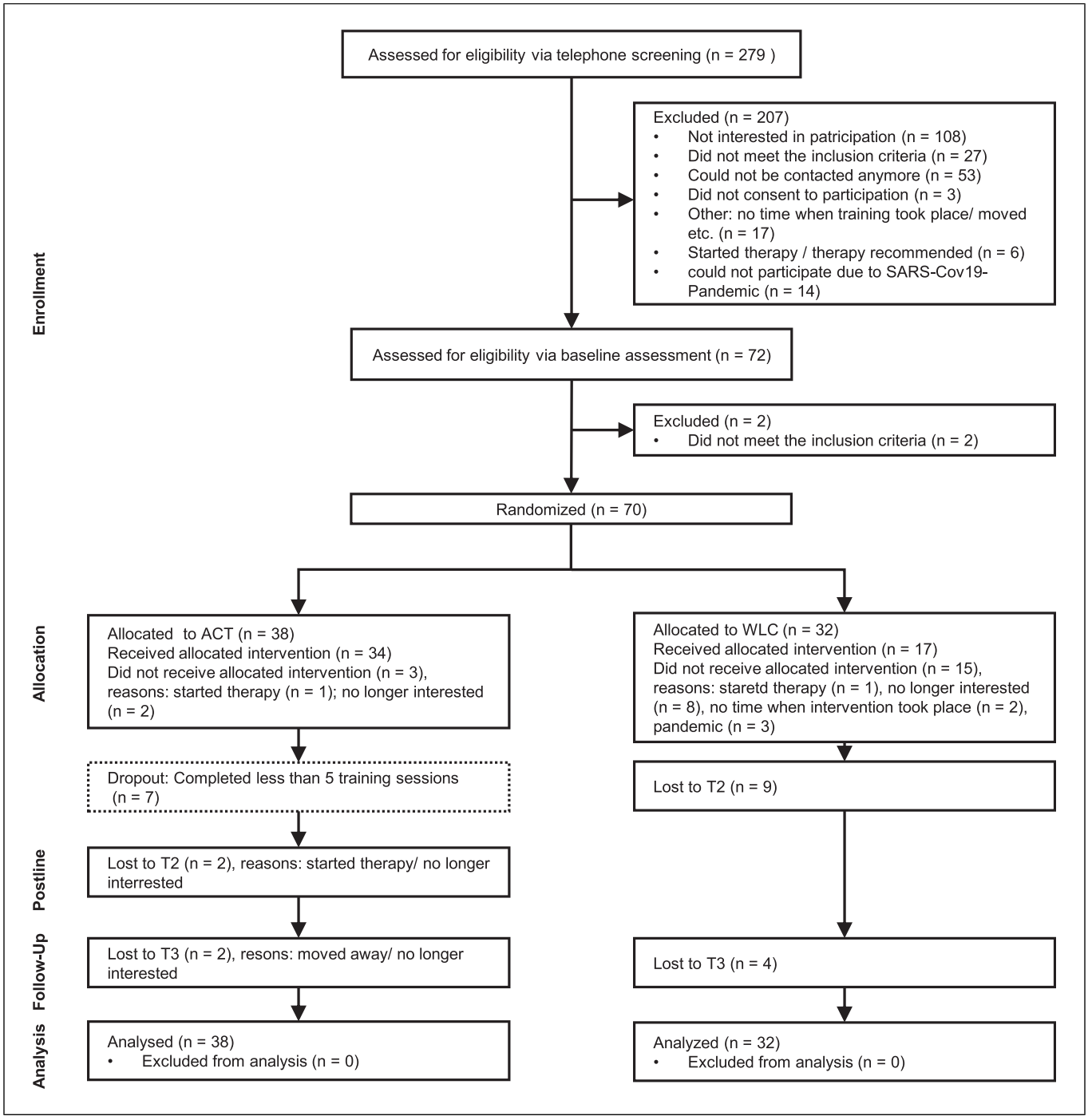

Fig. 1. Participant flow chart. ACT, acceptance, and commitment therapy group; WLC, waitlist control group.

means, standard deviations, and pre-post correlations in the intervention and control groups. Results showed that a sample size of 72 participants would be necessary to reveal an interaction effect of TIME and GROUP with a statistical power of beta = 0.8 and an alpha level of 0.05. Due to the altered population of interest as well as expected dropouts, we initially aimed for a sample size of n = 100. Unfortunately, due to the outbreak of the COVID-19 pandemic, we had to stop recruiting and decided to close the trial at n = 70. Figure 1 shows the participant flow. Eligible participants were pupils aged 13–18 years attending school in Heidelberg and the

larger Rhine Neckar catchment area who showed elevated levels of stress (a score of 8 or higher) in an initial telephone-based screening using the Perceived Stress Scale 4 (PSS-4 [70, 71]). Students reporting severe psychiatric disorders requiring treatment (i.e., borderline personality disorder, severe depression, or schizophrenia) were excluded. In addition, students who received psychotherapeutic treatment at the time of screening or at any time during the study period were excluded.

Cohorts of a maximum of 20 individuals were recruited for each starting ACT group (max. 10 per group). Unfortunately, one last cohort with 14 participants could not be finalized due to the COVID-19 pandemic outbreak in spring 2020. After interested students or their parents/legal guardians had established first contact with study-staff members, the telephone-based screening was conducted. If participants were eligible for participation in the trial, adolescents and their parents received written information material and declarations of consent. Written consent of both the parents/legal guardians and the adolescent was obtained prior to further study appointments. Data collection was performed by a trained clinical psychologist who was blinded to intervention group allocation and comprised three appointments at different time points: baseline (T1); post-intervention after intervention (ACT) or waiting list (WLC), respectively (T2); and follow-up (ACT) or post-intervention (WLC), respectively (T3). Primary outcome was perceived stress measured with the Perceived Stress Scale (PSS-10 [70]) at T2 (after the training in the intervention group and before the training in the WLC group). Participants received an allowance of EUR 20 for each appointment of the data collection. The training lasted 10 weeks, divided into 8 group sessions of 90 min each. Participants who attended less than five sessions of the training were marked as treatment dropouts. The training was based on a manual which is described in detail elsewhere [72]. More detailed information on the recruitment of participants and the data collection can be found in the online supplementary material (OSM).

Measures

Interviews and Questionnaires

At T1, the standardized International Neuropsychiatric Interview for Children and Adolescents (MINI-Kid [73]) and the borderline personality disorder (BPD) section of the Structured Clinical Interviews for DSM-IV (SKID-II [74]) were conducted. Participants were excluded and referred to appropriate clinical treatment if they fulfilled diagnostic criteria for one of the mental disorders defined as exclusion criteria. If none of the exclusion criteria were met, participants completed baseline data collection.

Several computer-based (LimeSurvey) questionnaires were completed at each timepoint. At T1, this assessment was carried out immediately after the interview; at T2 and T3, data were collected at the beginning of the appointment.

The PSS-10 [70] was used to measure perceived levels of stress within the last month. The primary endpoint was a priori defined as the PSS-10 score at T2. The School Burnout Inventory (SBI [20]) was used to measure symptoms of school burnout. The Children's Somatization Inventory (CSI, [75]) was used to assess somatic stress-related symptoms. Psychological flexibility was measured with the Acceptance and Fusion Questionnaire for Youth (AFQ-Y [76]). The Strengths and Difficulties Questionnaire (SDQ [77]) was used as additional measure addressing the severity of psychopathology. Furthermore, we assessed health-related quality of life using the KIDSCREEN-10 [78].

Following the training (at T2), we conducted an assessment of the participants' satisfaction with the training using an adapted version of the *Fragebogen zur Patientenzufriedenheit* (ZUF-8 [79]). The questionnaire has a possible range of the total score from 8 to 32. Unlike all other data, this questionnaire was collected immediately after the last training session by the respective trainers.

Hair Cortisol

A hair sample was taken to determine cortisol as a physiological correlate of stress. When collecting the hair samples, we followed the recommendations described elsewhere [80]. More information can be found in the OSM.

Ecological Momentary Assessment

The present level of stress was further measured using ecological momentary assessment (EMA). At T1, T2, and T3, participants received smartphones to assess stress in their everyday life during a usual school week. EMA via study smartphones makes it possible to capture behaviors and experiences in real time in the natural environments without delay through repeated measurement [81]. Data were collected over 5 days (Monday to Friday), 2 weeks prior to the beginning of the intervention group's training, 2 weeks prior to the beginning of the control group's training, and after the control group's training. Within one school week (Monday to Friday), the participants were asked to answer questions concerning their perception of daily-life stress three times a day according to their individual school schedule in the morning, after school, and before they went to bed. The questions were based on the PSS and supplemented by additional questions concerning the causes of stress as well as current mood and sleeping quality. More information can be found in the OSM.

Randomization and Intervention

Following T1, participants were block-randomized to either the ACT or the WLC group by an independent researcher who was not involved in data collection or the implementation of the training. Personnel involved in data collection were blinded regarding the outcome of the randomization and allocation of participants. The trainers informed participants which group they were allocated to. Half of the cohort then started the stress-prevention training.

Intervention

The training took place on the premises of Child and Adolescent Psychiatry, but separately from where the data were collected. Two existing manuals provided the basis for the training [82, 83]. The stress-prevention intervention was based on the principles of ACT [39]. In addition, psychoeducation on stress and its physical and psychological implications are part of the training. Training in problem solving is an important component of the concept. Another characteristic of the manual are creative elements; throughout the session, the adolescents are often invited to draw metaphoric images, e.g., of their mind, or to design a collage about their individual values. These art therapy techniques were adapted from an earlier manual [82] and were

considered helpful since they provide non-linguistic access to the concepts and metaphors of ACT. Problem-solving strategies as provided in the manual by Livheim [83] were integrated as a helpful and empirically proven addition to acceptance to be used in constellations where the external situation can be changed to improve wellbeing. Each training group consisted of 3–10 participants and was led by two trainers. The intervention comprised 8 sessions of 90 min each. In the beginning of the training, the sessions took place on a weekly basis. The last two sessions were held with an interval of 2 weeks to facilitate the transfer into everyday life (booster sessions). The two booster sessions were chosen to allow for a greater transfer to everyday life and more sustainable changes, as suggested by some authors in the context of stress prevention [84, 85]. During school holidays, interventions were on hold. An overview over the sessions can be found in the OSM (S1). The training realizes central concepts of ACT and emphasizes different aspects of these core principles in each session. First, the trainers try to create an atmosphere of trust. The exchange between the participants, as well as the trainers, regarding individual difficulties and also about ways to deal with stressful events is an important basis of the group concept. The adolescents are taught several exercises to employ strategies to deal with difficult thoughts, feelings and physical perceptions in their everyday life.

Statistics

Descriptive statistics were calculated to illustrate sample characteristics and group differences. First, systematic differences on sociodemographic and clinical variables of interest between the ACT group and the WLC group were analyzed at T1. Chi-square tests of group differences were calculated concerning discrete variables and two-tailed *t* tests concerning continuous variables. We used the same procedure to analyze possible systematic differences at the baseline level between dropouts and participants who remained in the study (completer). Main analyses followed a three-step approach. First, we investigated main effects of the intervention at the primary endpoint (T2) using a one-tailed *t* test for independent groups as per the trial registration. Further, we assessed the effect size using Cohen's d. The reduction of perceived stress (PSS-10) at T2 was the primary outcome as preregistered. Second, in exploratory analyses, we used mixed linear effect models investigating main effects of TIME and GROUP as well as their interaction on the dependent variables of interest in the intention to treat (ITT) sample as randomized. The respective models used the individual subject ID as a random effect, comparing trajectories in both groups across all repeated measures (T1, T2, T3). Sidak-corrected contrasts were derived to estimate main and interaction effects. Third, to account for the control group having received the intervention between T2 and T3, and to address the stability of effects, we ran mixed linear regression models investigating main effects of the INTERVENTION (T2 and T3 in the intervention group, T3 in the control group) and carry-over effects of the intervention during FOLLOW-UP (T3 in the intervention group only), alongside the main effects of TIME and GROUP in the ITT sample. Again, subject ID was used as a random effect in the respective models. Differences in participant satisfaction were assessed using two-tailed *t*-tests for independent groups alongside descriptive statistics. Data was analyzed with Stata/SE (16.0; Stata Corp. LLC, College Station, TX, USA) and at an alpha-level of 0.05.

Results

Table 1 provides an overview of the sociodemographic and clinical sample characteristics at T1. Descriptive statistics at different time points (T1–T3) for both groups are displayed in the OSM (S2). There were no significant differences between ACT and WLC groups at the baseline assessment. No participant was excluded due to diagnoses predefined as exclusion criteria.

Primary Outcome: PSS

Regarding the main hypothesis, the ACT group showed significantly lower levels of perceived stress compared to the WLC group at T2 ($t(65) = 3.13$, $p = 0.001$), with a medium-to-large effect size of $d = 0.77$. Further, mixed models yielded no significant main effects of TIME or GROUP, but a significant TIME by GROUP interaction ($\chi^2(2) = 15.48$, $p < 0.0001$), indicating different trajectories in PSS levels over time in the ACT group compared to the WLC group. Further analyses accounting for the WLC having received the intervention with a time-lag yielded significant results for INTERVENTION ($\beta = -5.31$, $p < 0.0001$) and TIME (T2: $\beta = 3.33$, $p = 0.001$; T3: $\beta = 5.84$, $p = 0.004$), but no significant INTERVENTION × TIME interaction. A graphical representation of the PSS total score at all assessment time points can be found in the OSM (S3).

Exploratory Analyses and Secondary Outcomes

Since the main hypothesis was confirmed, further analyses followed the explorative approach outlined earlier. Detailed information about the trajectories in both groups across all repeated measures is provided in Table 2.

For SBI, Sidak adjusted contrasts yielded no significant main effects but a significant TIME-by-GROUP interaction ($\chi^2(2) = 7.41$, $p = 0.025$), indicating a different trajectory in SBI levels over time in the ACT group compared to the WLC group: a reduction of the SBI scores in the ACT condition from T1 to T2, whereas the SBI scores were elevated in the WLC condition. Further analyses accounting for the WLC having received the intervention time-delayed only yielded a significant result for INTERVENTION ($\beta = -0.49$, $p = 0.01$), indicating that the WLC group showed a reduction of school burnout symptoms after the subsequent training as well.

Regarding the CSI, Sidak adjusted contrasts yielded no significant main effects, but again a significant TIME × GROUP interaction (χ^2 (2) = 10.32, $p = 0.006$), indicating a different change in CSI levels over time in the ACT group compared to the WLC group. Further

Table 1. Sociodemographic and clinical sample characteristics at T1

Sociodemographic variable/diagnostic category	WLC (n = 32)	ACT (N = 38)	Group differences, p value
Mean age (SD), years	15.47 (1.65)	15.13 (1.6)	0.389
Sex, n (%)			
Female	27 (84.44)	29 (76.32)	
Male	5 (15.63)	9 (23.68)	0.401
School type, n (%)			
Secondary school	6 (18.75)	7 (18.42)	
High school	24 (75)	30 (78.95)	
Others	2 (6.25)	1 (2.63)	0.753
MINI-Kid diagnosis[1], n (%)			
F1 Section (ICD-10 GM)	2 (6.25)	0 (0)	0.118
F3 Section (ICD-10 GM)	1 (3.12)	3 (7.89)	0.524
F4 Section (ICD-10 GM)	12 (37.5)	8 (21.05)	0.128
F9 Section (ICD-10 GM)	2 (6.25)	1 (2.63)	0.456
No diagnosis	19 (59.38)	28 (73.68)	
Regular intake of any medication	6 (18.75)	6 (15.79)	0.743
PSS, mean (SD)	17.63 (4.8)	18.45 (5.87)	0.528
SBI, mean (SD)	3.18 (0.71)	3.35 (0.87)	0.370
CSI, mean (SD)	16.56 (9.0)	19.5 (13.5)	0.300
AFQ, mean (SD)	18.53 (8.65)	19.11 (10.11)	0.801
SDQ, mean (SD)	11.88 (5.48)	11.08 (4.55)	0.509
KIDSCREEN-10, mean (SD)	43.76 (6.69)	44.64 (7.59)	0.612
Cortisol[2], mean (SD)	6.25 (16.21)	3.51 (2.53)	0.335

[1]Multiple diagnoses per subject possible. MINI-KID, International Neuropsychiatric Interview for Children and Adolescents [73]; ICD-10 GM, International Classification of Diseases, German Modification [86]; PSS, Perceived Stress Scale [70]; SBI, School Burnout Inventory [20]; CSI, Children's Somatization Inventory [75]; AFQ, Acceptance and Fusion Questionnaire [76]; SDQ, Strengths and Difficulties Questionnaire [77]; KIDSCREEN-10 [78]. WLC, waitlist control group; ACT, acceptance and commitment therapy group. [2]Since not all participants provided hair samples, sample sizes for baseline cortisol are n (WLC) = 31 and n (ACT) = 34.

analyses yielded significant results for INTERVENTION ($\beta = -6.64$, $p = 0.005$), FOLLOW-UP ($\beta = -6.76$, $p = 0.007$), and TIME (T2: $\beta = 4.99$, $p = 0.004$; T3: $\beta = 10.79$, $p = 0.002$). There was a large increase in the WLC group between T1 and T2, while the ACT groups' levels decreased. After the WLC received the training, they still showed higher levels of somatization than the adolescents in the ACT condition, even though there was a reduction from T2 to T3.

Regarding all other outcomes (KIDSCREEN-10, AFQ, SDQ, Cortisol, EMA data), mixed models did not yield significant results. The evaluation of the participants' satisfaction with the intervention resulted in an average overall score of 26.06 (SD 3.02) in the ACT-, average overall score of 26.18 (SD 3.13) in the WLC-, and average overall score of 26.10 (SD 3.03) in the whole sample. There was no significant difference between the groups regarding satisfaction with the intervention ($t(49) = 0.13$, $p = 0.898$).

Discussion

The aim of this RCT was to systematically evaluate the effects of a new group intervention for adolescents suffering from high levels of perceived stress based on the principles of ACT. To our knowledge, this is the first RCT with a sufficient sample size addressing adolescents with elevated stress levels in the form of an indicated prevention. Different from most research conducted in the field, the present RCT directly addressed adolescents with high stress levels, not adolescents affected by conditions which might imply a high burden of stress.

As hypothesized, adolescents in the ACT group reported significantly lower levels of perceived stress at the primary endpoint, confirming the efficacy of the training. The WLC group also profited from the training which was delivered time delayed. Furthermore, the training was effective in the reduction of symptoms of school burnout and in the reduction of physical stress-associated

Table 2. Mixed models: trajectories in both groups across all repeated measures

Outcome	Wald χ^2	p value (χ^2)	Sidak adjusted contrasts					
			time		group		time × group	
			χ^2	p value	χ^2	p value	χ^2	p value
PSS	17.72	0.003	1.42	0.491	1.46	0.228	15.48	>0.01
SBI	11.61	0.041	4.46	0.107	0.01	0.929	7.41	0.025
CSI	12.08	0.034	1.98	0.371	0.37	0.546	10.32	0.006
AFQ	3.14	0.678	1.35	0.510	0.14	0.709	1.69	0.429
SDQ	11.14	0.049	10.2	0.006	0.87	0.352	0.19	0.911
KIDSCREEN-10	7.51	0.185	5.12	0.077	0.84	0.358	1.99	0.370
Cortisol	7.87	0.164	5.12	0.077	1.05	0.305	2.28	0.319
Stress (EMA)	5.11	0.403	3.18	0.204	0.03	0.864	1.85	0.396
Affect (EMA)	6.15	0.292	3.93	0.140	0.61	0.433	1.67	0.433
PSS (EMA)	7.46	0.188	5.45	0.066	0.4	0.525	1.58	0.454
Pressure (EMA)	21.67	0.001	16.58	<0.01	3.72	0.054	2.05	0.359
Teachers (EMA)	24.62	<0.01	15.73	<0.01	6.5	0.011	2.63	0.268
Future (EMA)	8.1	0.151	2.46	0.292	4.75	0.029	1.45	0.485
Friends (EMA)	1.89	0.864	0.14	0.932	1.34	0.248	0.59	0.743
Love issues (EMA)	4.61	0.465	2.61	0.271	0.18	0.673	1.99	0.370
Sleep (EMA)	4.1	0.535	3.67	0.160	0.02	0.898	0.35	0.841

PSS, Perceived Stress Scale [70]; SBI, School Burnout Inventory [20]; CSI, Children's Somatization Inventory [75]; AFQ, Acceptance and Fusion Questionnaire [76]; SDQ, Strengths and Difficulties Questionnaire [77]; KIDSCREEN-10 [78]; EMA, ecological momentary assessment.

symptoms. Surprisingly, there were no measurable changes in the other collected data (AFQ, SDQ, KIDSCREEN-10, Cortisol, EMA data). The outcomes of perceived stress, school burnout, and physical symptoms, which are known to be closely associated with stress, seem most suitable to track changes over the course of the study in the sample. It is rather surprising that the EMA data did not yield significant results. Other studies using EMA as a tool to collect data on stress also report differences between self-report data and EMA data [87] or between data collection in the laboratory versus at home [88]. Possible reasons for differences between EMA data and other self-report data discussed in the literature are, amongst others, a potential recall bias [89], altered self-awareness due to repeated assessments, and "retrospective reporting bias" [90, p. 1102]. Further, EMA data can potentially be biased by the tendency to skip assessment time points in EMA designs when busy or emotionally involved in everyday life or by technical problems [91].

A particular strength of the present study is the multimodal assessment of stress. Another positive aspect compared to existing studies on ACT for adolescent stress is the methodological quality. Methodological deficiencies of previous research (for an overview, see [50]) were largely eliminated. Unlike similar studies [e.g., [38, 51–53, 56, 57], where no such information was provided, the scientific personnel that collected the outcome data were blinded to the condition.

Earlier research conducted with different adolescent populations lends support to the assertion that ACT might provide a conceptual framework for interventions to prevent adolescent stress [51, 53]. It should be noted that, in this RCT, elements of ACT were enriched by other components such as psychoeducation on stress, problem-solving techniques, and art therapy. Given the particular effects of ACT, the trial is further limited by no active control group which accounts for unspecific factors (e.g., relationship, intervention dose). The fact that we did not find significant pre-post differences in AFQ might suggest that the effects of the intervention were not primarily driven by ACT elements. This should be the subject of future research.

The conclusions which can be drawn from the results of the present study may be limited due to the unequal sex distribution in the sample. However, it should be kept in mind that there is some evidence that female adolescents experience more perceived stress than their male peers [18, 19]. Another limiting factor might be the unequal distribution of school types in the sample with more than three-quarters of participants attending high school. Moreover, due to the WLC design, follow-up data is only available for the

IG. For this reason, the conclusions concerning long-term effects of the training are limited to a rather small sample and a limited period of observation. A longer follow-up period to obtain information regarding stability of the effects would be desirable for future research. Further, there were some feasibility issues illustrated by the ratio between the number of screened potential participants and the actual sample size. Working with a sample of stress-burdened adolescents seems to imply participants' difficulties in finding the time and the motivation for additional appointments, even if they are willing to reduce the problem itself. Implementation in practice should therefore offer high levels of flexibility and availability and a low threshold for the participants (e.g., providing flexible time slots directly within schools). Another limitation of the study – which particularly limits conclusions concerning specific effects of ACT in stress prevention – is the lack of an active control group. This aspect should be considered for future research. However, it should be noted that an active control group can be regarded as standard in psychotherapy research, but in prevention approaches, this lack is considered justifiable, as "no intervention" is commonly the "treatment as usual" in this population. In a recent meta-analysis conducted by our group on ACT-based interventions to reduce stress in children and adolescents [50], six of the ten included studies used either a WLC, or the control group continued their regular class activities or medication. Only three studies compared the intervention to TAU, e.g., regular support from the school or standard care at the clinic [55, 56, 83], and only one study conducted an active control condition that would not have taken place without the study [92].

The receipt of economic incentives might have affected the participants' motivation to partake in the study. However, the incentives were only provided for participation in study assessments, and not for participation in the intervention. A bias of the results due to this seems unlikely since both groups equally received the same allowance and participation in the training was not remunerated. In comparison, the efforts to attend the training were much higher than the appointments for data collection.

Overall, the present RCT provides important evidence regarding the efficacy of an indicated prevention approach for adolescents affected by high levels of perceived stress. Group-based indicated stress-prevention approaches might contribute to a reduction of allostatic load. Possible applications of the training might be school-based settings, e.g., in the context of school psychological counseling, or youth counseling centers. An adaptation to a psychotherapeutic outpatient setting is also conceivable. Further research should focus on the questions regarding generalizability of the findings to other samples, the underlying efficacy mechanisms, the stability of the effects over a longer period, and the optimization of the feasibility of indicated stress prevention in youth.

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Statement of Ethics

Approval of the Institutional Review Board (Ethics Committee) of the medical faculty at the University of Heidelberg was obtained before recruitment (Study ID: S-014/2017). All participants and parents/legal guardians (if participants were below age 18) provided written informed consent. Written informed consent was obtained from the participants' parent/legal guardian/next of kin to participate in the study for all vulnerable patients. The study was conducted in accordance with the Declaration of Helsinki.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

F.B. was involved in the study design, carried out data acquisition including recruitment and assessment, performed statistical analyses, and wrote the manuscript. J.K. acquired funding, performed statistical analyses, and was involved in the study design and supervision. M.K. acquired funding, was responsible for the conception, design, and coordination of the work. F.R. was involved in the study design and supervision. All authors revised the article critically, gave final approval of this version to be published, and agree to be accountable for all aspects of the work.

Data Availability Statement

The data that support the findings of this study are not publicly available due to their containing information that could compromise the privacy of research participants but are available from the corresponding author [M.K.; Michael.kaess@upd.ch] upon reasonable request. Further inquiries can be directed to the corresponding author.

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