Depression in adolescents: Feasibility, efficacy, and neural correlates of a brief group psychotherapeutic treatment, along with insights on epidemiology, symptoms, and diagnostics

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<th>Description</th>
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</thead>
<tbody>
<tr>
<td>ACC</td>
<td>anterior cingulate cortex</td>
</tr>
<tr>
<td>BAT</td>
<td>behavioural activation therapy</td>
</tr>
<tr>
<td>BDI-II</td>
<td>Beck Depression Inventory-Revision</td>
</tr>
<tr>
<td>CAR</td>
<td>cortisol awakening response</td>
</tr>
<tr>
<td>CBT</td>
<td>cognitive behavioural psychotherapy</td>
</tr>
<tr>
<td>CBT-G</td>
<td>group cognitive behavioural therapy</td>
</tr>
<tr>
<td>CDRS-R</td>
<td>Children’s Depression Rating Scale-Revised</td>
</tr>
<tr>
<td>CWD-A</td>
<td>Coping With Depression course for Adolescents</td>
</tr>
<tr>
<td>DSM</td>
<td>Diagnostic and Statistical Manual of Mental Disorders</td>
</tr>
<tr>
<td>fMRI</td>
<td>functional Magnetic Resonance Imaging</td>
</tr>
<tr>
<td>ICD</td>
<td>International Classification System of Diseases</td>
</tr>
<tr>
<td>IPT</td>
<td>interpersonal psychotherapy</td>
</tr>
<tr>
<td>IPT-A</td>
<td>interpersonal psychotherapy for depressed adolescents</td>
</tr>
<tr>
<td>MDD</td>
<td>major depressive disorder</td>
</tr>
<tr>
<td>MICHI</td>
<td>Manualized Intervention to Cope with depressive symptoms, Help strengthen resources and Improve emotion regulation</td>
</tr>
<tr>
<td>PASCET</td>
<td>Primary and Secondary Control Enhancement Training</td>
</tr>
<tr>
<td>PAT-I</td>
<td>Depressed adolescent patients (PAT) assigned to the intervention group (I)</td>
</tr>
<tr>
<td>PAT-W</td>
<td>Depressed adolescent patients (PAT) assigned to the wait-list control group (W)</td>
</tr>
<tr>
<td>RCT</td>
<td>randomized controlled trial</td>
</tr>
<tr>
<td>sgACC</td>
<td>subgenual anterior cingulate cortex</td>
</tr>
<tr>
<td>SSRI</td>
<td>selective serotonin reuptake inhibitor</td>
</tr>
<tr>
<td>TAU</td>
<td>psychiatric treatment as usual</td>
</tr>
<tr>
<td>vACC</td>
<td>ventral anterior cingulate cortex</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
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<td>WL</td>
<td>wait list</td>
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Abstract

At the time the present research was started, the treatment of depression in adolescents in Germany was only addressed by a small number of structured intervention programs. However, none of these combined the advantages of a cognitive behavioural treatment that is brief, is applied in a group setting, is intended to treat all levels of severities of depression, and has been evaluated with respect to acceptance, feasibility, and efficacy. Furthermore, no investigations had been done on neural correlates of psychotherapeutic treatment of depression in adolescents. To address all these issues, we developed a brief cognitive-behavioural group psychotherapy for depressed adolescents titled “Manualized Intervention to Cope with depressive symptoms, Help strengthen resources and Improve emotion regulation” (MICHI). In two pilot studies, one conducted in inpatients and the other in outpatients, MICHI was shown to be feasible and accepted, and to reveal first trends of efficacy. In a subsequent randomized controlled trial, depressed adolescent patients were assigned to either an intervention group that received MICHI (PAT-I) or a wait-list control group that received treatment as usual (PAT-W). Results indicated a significant interaction effect between groups (PAT-I/PAT-W) and time-points of measurement (pre/post), with small to moderate effect sizes seen in reduction of depressive symptoms.

Neural correlates of the psychotherapeutic interventions were investigated using functional Magnetic Resonance Imaging (fMRI). In the PAT-I group, pre-to-post symptom changes were found to be significantly associated with changes in activity in the subgenual anterior cingulate cortex (sgACC), the amygdala, and the hippocampus, all brain areas that are closely associated with depression. Post hoc analyses revealed a significant interaction effect between groups (PAT-I/PAT-W) and time points of measurement (pre/post) for the bilateral sgACC, the left amygdala, and the left hippocampus. Additionally, bilateral sgACC activity before treatment correlated significantly with subsequent pre-to-post symptom improvement in PAT-I.

Further analyses were aimed at acquiring new insights into the epidemiology, symptoms, and diagnostics of affective disorders in adolescents, as follows: 1) An examination of trends in inpatient treatment in Germany for depressive disorders in adolescents between 2003 and 2012 found that admissions increased over this period, which highlights the need for fast and efficacious help. A frequent reason for referral to inpatient treatment is acute suicidality, whose underlying contributing factors are still not fully understood in minors.
2) Results of our study indicated that symptoms of mania have a predictive value when it comes to suicidality, even after controlling for depression scores. This underscores the need for valid diagnostic instruments for the assessment of mental health symptoms. 3) For the assessment of depression in minors, the structured interview most frequently used in clinical and research contexts is the Children’s Depression Rating Scale-Revised (CDRS-R). Up to now, it was not known how the sum scores in the CDRS-R are associated with severity of depression as assessed by the International Classification System of Diseases (ICD-10), which is important for recognizing depressive disorders and being able to refer patients for proper treatments. Our study determined a cut-off score of 36 on the CDRS-R to be indicative of a mild to moderate depressive episode. 4) Another frequently used diagnostic self-report instrument is the Beck Depression Inventory-Revision (BDI-II), but it was unclear how similar this is to the CDRS-R for measuring symptoms of depression in minors. Accordingly, the two instruments were compared, and were found to correlate highly in scores, specifically on the symptom level, with the item of suicidality having the highest correlation.
German Summary/Zusammenfassung


Weitere Studien verfolgten das Ziel neue Einblicke in die Epidemiologie, Symptomatik und Diagnostik von affektiven Störungen bei Jugendlichen zu erlangen: 1) Eine Untersuchung welche Anzahlen, der wegen depressiven Episoden im stationären Setting behandelten Jugendlichen zwischen 2003 und 2012 in Deutschland verglich, ergab einen Anstieg über die
1. General Introduction

1.1. Epidemiology of depressive disorders in adolescents

With respect to age of onset of depression, first episodes are sometimes seen in childhood but more commonly in early or middle adolescence (Groen & Petermann, 2008). Individuals who meet the criteria for a major depressive disorder for the first time in adolescence (Fombonne, Woster, Cooper, Harrington & Rutter, 2001) are at higher risk (62.4%) for recurrence in adulthood. Studies have found a wide variation in the duration of depressive episodes, with a mean length of approximately eight months (Mehler-Wex, 2008). However, Patton et al. (2014) found that if episodes of depression in adolescents last longer than six months, symptoms often persist until adulthood, which highlights the need for prompt and effective treatments during adolescence that keep episodes as short as possible.

In German children of elementary school age, lifetime prevalence rates of depressive disorders are assumed to range from 1% to 2%, with an equal distribution between the sexes; however, this may differ from the prevalence rates in other countries (Groen & Petermann, 2008). In adolescents aged 13 to 18 years, the prevalence rate of depressive episodes that last from 1 to 12 months is 5.6% (Costello, Erkanli & Angold, 2006), with the rate in this age group being higher for girls (5.9%) than for boys (4.6%). Based on the findings of 17 European studies, the prevalence rates of depression in adults range from 3.1% to 10.1% (median: 6.9%) (Wittchen & Jacobi, 2005). As adolescents get older, their overall prevalence rates of depression become more and more comparable to those of adults.

According to the World Health Organization (WHO), depression is expected to be the most frequent disorder in industrialized countries by 2030 (Allianz Deutschland, 2011) and a comparison of prevalence rates of depression in adults between 2004 and 2008 revealed an increase of 23%. However, little research exists on whether prevalence rates of depressive disorders in minors rose within this time frame as well. In one meta-analysis, which included all studies that had used structured interviews to assess depressive disorders in children and adolescents born between 1965 and 1996, Costello et al. (2006) found no evidence for an increasing prevalence of depressive disorder over this time period. However, two other studies looked at whether there were changes over time in the prevalence rates for the broader concept of emotional problems, comprising questions about sorrows, sadness,
Epidemiology of depressive disorders in adolescents

reduced self-esteem, and anxiety. One study of three British birth cohorts born in 1974, 1986, and 1999 found a trend-wise increase in emotional problems (Collishaw, Maughan, Goodman & Pickles, 2004), and a German study that assessed psychopathological problems in children and adolescents at two time points, 2003–2006 and 2009–2012, found a slight increase of emotional problems in the age group of 11- to 17-year-olds (Hoelling et al., 2014). Thus, while prevalence rates for depressive disorders in children and adolescents did not change over time, prevalence rates for emotional problems did.

Despite the finding of no increase in prevalence rates for depression, the number of antidepressants being prescribed for children and adolescents has been increasing (Zito et al., 2003); specifically, prescriptions for selective serotonin reuptake inhibitors (SSRIs) and hypericum (Fegert, Koelch, Zito, GlAESKE & Janhsen, 2006). Furthermore, in Germany, it has been found that outpatient treatment diagnoses of depressive disorders in children and adolescents under the age of 15 years rose about 16% from 2005 to 2008 (Annuss et al., 2010). These increases in pharmaceutical treatment and outpatient treatment might reflect increased help-seeking behaviour, improved diagnostic skills at the primary care level, more openness to seeking help, or an improved health supply in general (Hegerl, 2013). To date, there exists one study of Holtmann et al. (2010) that examined national trends in the rates of inpatients between 2000 and 2007. Results indicate increased rates of inpatients up to 19 years that were diagnosed with depressive disorder. However following our knowledge newer studies are missing. Inpatient treatment is especially relevant for severely affected minors suffering from an acute crisis (e.g., acute suicidality) whose very low psychosocial functioning level might prevent them from attending school, and for those whose symptomatology is closely related to family dysfunction.

In summary, prevalence rates for depressive disorders increase from childhood to adolescence, reaching levels in older adolescents that are similar to those seen in adults. Despite no increase in the overall prevalence of depressive disorders, increases have been seen in the numbers of both psychopharmacological prescriptions and of outpatients being treated for depressive disorders. However there are newer studies missing about whether those rising numbers of out- and inpatients are still rising. The high relapse rate in adulthood in individuals whose first depressive episode occurred during adolescence highlights the need for more studies investigating effective treatments in this age group.
1.2. Classification of symptoms

In about 40% of cases, depression is accompanied by one or more co-morbidities (Essau, Conradt & Petermann, 2000) such as anxiety disorders, eating disorders, substance abuse, and attention deficit hyperactivity disorder (ADHD) (Bettge et al., 2008). In children and adolescents, depression is also often accompanied by problems such as irritable mood, loss of interest in school, and decline in academic performance (Mehler-Wex, 2012). Taken together, all those aspects affect family and school life as well as personal relationships. Given the nature and associated risks of depression, the Global Burden of Disease Study of the WHO (Vos, Flaxman, Naghavi, Lozano & Michaud, 2012) has identified it as one of the most debilitating disorders worldwide.

A depressive disorder may be diagnosed using either the Diagnostic and Statistical Manual of Mental Disorders (DSM) or the International Classification System of Diseases (ICD). Both specify that symptoms must last at least two weeks, but they differ in that DSM-5 (American Psychiatric Association, 2013) says only that at least five symptoms must be fulfilled in order for a diagnosis of a major depression to be made, while ICD-10 specifies the fulfillment of four, six, or eight symptoms for the diagnosis of mild, moderate, or severe depressive disorder, respectively (Remschmidt, Schmidt & Poustka, 2009). The only change from DSM-IV (American Psychiatric Association, 1994) to DSM-5 (American Psychiatric Association, 2013) has been removal of the previously exclusion criterion of depressive symptoms lasting less than two months following the death of a loved one. Therefore, assessment instruments referring to previous classification systems for diagnosing a depressive disorder can still be applied.

In both the ICD-10 (Remschmidt, et al., 2009) and the DSM-5 (American Psychiatric Association, 2013), the main symptoms of a depressive episode are low mood, reduced energy, and decreased activity. Other common symptoms include reduction in the capacity for enjoyment, interest, concentration, marked tiredness, sleep disturbance, diminished appetite, feelings of guilt or worthlessness, and (in ICD-10 only) reduced self-esteem. Other symptoms of depressive disorders are elevated levels of suicidal ideation, suicidal behaviour, and completed suicide (Nock et al., 2013); the last being among the most common causes of death in European adolescents (Wilkinson, Kelvin, Roberts, Dubicka & Goodyer, 2011). Among US adolescents, lifetime prevalence rates for suicidal ideation, plans, and attempts have been found to be 12.1%, 4.0%, and 4.1%, respectively (Nock et al., 2013); while in
Instruments for diagnosing depression in adolescents

Germany, more than a third of adolescents have reported having had suicidal ideation at some point (Donath, Graessel, Baier & Hillemacher, 2013; Plener, Kapusta, Fegert & Keller, 2009). Suicidal ideation and attempts are seen more frequently in females (Kokkevi, Rotsika, Arapaki & Richardson, 2012), but completed suicide is more frequent in males (Värnik et al., 2009).

The category of affective disorders (F3) in ICD-10 also includes bipolar disorders, which are characterized by alternating depressive and (hypo-) mania episodes, and have a prevalence rate of 2.1% among 15- to 18-year-olds (Kozloff et al., 2010). In about 9 out of 10 adolescents, bipolar disorders start with a depressive episode and about 10% of depressed adolescents develop a (hypo-) mania episode within ten years (Birkle & Holtmann, 2014). Like depressive disorder, bipolar disorder has been shown to be associated with elevated levels of suicidal behaviour (Allison, Roeger, Martin & Keeves, 2001; Brent et al., 1993), especially in the case of an early onset (Van Meter, Moreira & Youngstrom, 2011). The criteria for bipolar disorder have been found to be fulfilled at least once by 9.1% of those reporting lifetime suicidal ideation, by 13.2% of those reporting a lifetime suicide attempt (Nock et al., 2013), and by 17.9% of those who actually committed suicide (Brent et al., 1993). However, there is little knowledge about whether the extent for suicide risk is higher in adolescents with symptoms of both mania and depression compared to those with depressive symptoms alone.

In sum, the two classification systems use similar symptoms for diagnosing a depressive disorder, but the ICD-10 allows the classification of episodes into different levels of severity. Suicidal ideation is a devastating symptom of depression, with a high prevalence rate in the general adolescent population and an even higher one in the depressed adolescent population. Accordingly, better understanding is needed of predictors for suicide in adolescents, including whether symptoms of mania in addition to those of depression predict suicidal ideation and behaviours more strongly than do depressive symptoms alone.

1.3. **Instruments for diagnosing depression in adolescents**

As a foundation for determining the most suitable treatment, diagnostic instruments that can appropriately detect the presence and severity of a depressive episode are necessary. In Germany, the guidelines for the treatment of depression in adults (Deutsche Gesellschaft für Psychiatrie Psychotherapie und Nervenheilkunde, 2009) state that questionnaires should be
Instruments for diagnosing depression in adolescents

used for the early detection of depressive symptoms, and that the nature of the symptoms as well as their severity and duration should be explored by means of structured interviews in order to make a valid diagnosis. The level of recommendation for this is “B”, meaning that the recommendation is based on knowledge derived from non–randomized controlled trials (RCT). Following the German guidelines for the treatment of depression in children and adolescents issued by the “Deutsche Gesellschaft für Kinder- und Jugendpsychiatrie Psychosomatik und Psychotherapie” (2013) clinical assessment and diagnosis should only be provided by clinical experts (level of recommendation: consensus). Table 1 lists self-rating scales, structured interviews, and parental questionnaires that have been designed specifically for the assessment of depression in children and adolescents.

Table 1 Questionnaires and structured interviews for the assessment of depression in adolescents

<table>
<thead>
<tr>
<th>Diagnostic instruments</th>
<th>Authors</th>
<th>Age range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beck Depression Inventory- Revision (BDI-II) ¹</td>
<td>Hautzinger, Keller &amp; Kühner (2006)</td>
<td>13 years to adulthood</td>
</tr>
<tr>
<td>Children’s Depression Inventory (CDI; CDI2) ¹/“Depressionsinventar für Kinder und Jugendliche”</td>
<td>Kovacs (1992, 2010); Stiensmeier-Pelster, Schürmann &amp; Duda (2000)</td>
<td>7–17 years</td>
</tr>
<tr>
<td>The depression test for children/ “Depressionstest für Kinder”</td>
<td>Rossmann (2005)</td>
<td>9–15 years</td>
</tr>
<tr>
<td>Center for Epidemiological Studies Depression scale (CES-D) ¹/ Allgemeine Depresionsskala (ADS)</td>
<td>Hautzinger, Bailer, Hofmeister &amp; Keller (2012)</td>
<td>13 years to adulthood</td>
</tr>
<tr>
<td>Self report questionnaire-depression/“Selbstbeurteilungsbogen für Depressionen” (SBB-DES)</td>
<td>Döpfner, Görtz-Dorten, Lehmkuhl, Breuer &amp; Goletz (2008)</td>
<td>11–18 years</td>
</tr>
<tr>
<td>Children’s Depression Scale</td>
<td>Lang &amp; Tisher (1978, 1983)</td>
<td>7–18 years</td>
</tr>
<tr>
<td>Depression Self-Rating Scale</td>
<td>Birleson (1981)</td>
<td>8–14 years</td>
</tr>
<tr>
<td>Carroll Self-Rating Scale</td>
<td>Carroll, Feinberg &amp; Smouse (1981)</td>
<td>&gt;18 years</td>
</tr>
<tr>
<td>Hamilton Rating Scale for Depression ¹</td>
<td>Williams (1988)</td>
<td>16 years</td>
</tr>
<tr>
<td>Montgomery-Asberg Depression Rating Scale</td>
<td>Montgomery &amp; Asberg (1979)</td>
<td>&gt;18 years</td>
</tr>
</tbody>
</table>
Instruments for diagnosing depression in adolescents

<table>
<thead>
<tr>
<th>Instrument</th>
<th>Authors</th>
<th>Age Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children’s Depression Rating Scale-Revised (CDRS-R)</td>
<td>Keller, Grieb, Koelch &amp; Sproeber (2012), Poznanski &amp; Mokros (1996)</td>
<td>6-18 years</td>
</tr>
<tr>
<td>Parent rating scale for depression/</td>
<td>Doepfner et al. (2008)</td>
<td>11-18 years</td>
</tr>
<tr>
<td>“Fremdbeurteilungsbogen für Depressionen”</td>
<td></td>
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</table>

Notes 1 = version available in German and English

Of the instruments available, the ones most widely used (Mayes, Bernstein, Haley, Kennard & Emslie, 2010; Subica et al., 2014) are the Children’s Depression Rating Scale-Revised (CDRS-R) and the Beck Depression Inventory- Revision (BDI-II).

The CDRS-R is a semi-structured structured interview that is leaned on the Hamilton Rating Scale for Depression - a structured interview that is frequently used for diagnosing depression in adults- which in turn is based on the DSM-IV criteria for depression. It was originally developed in the 1970s in the United States; was reworked in the 1980s (Poznanski & Mokros, 1996); and is now available in German (Keller et al., 2012). It contains 17 items, three of which are used to measure nonverbal aspects such as manner of speaking. Overall, the CDRS-R reveals good psychometric properties, including a high internal consistency (α=.85), a good test-retest reliability after one week (r=.92), and high inter-rater reliability (r=.95) (Keller et al., 2012). International studies on depression in adolescents that have used CDRS-R scores as inclusion criteria have employed different cut-offs, ranging from ≥36 in the Treatment of Adolescent Suicide Attempters Study (Brent et al., 2009) to ≥45 in the Treatment for Adolescent with Depression Study (Treatment for Adolescents With Depression Study Team, 2007). The latter aimed to include only subjects with depression rated as moderate to severe. Following the clinical experience of Guo, Nilsson, Heiligenstein, Wilson and Emslie (2006), CDRS-R total scores of below 20, 20–30, 30–40, 40–60, and over 60 correspond to no depression and to borderline, mild, moderate, and severe depression, respectively. However to date, no study has assessed scientifically how CDRS-R scores, of the German version, correlate with severity levels of depression as assessed by means of the ICD-10.

The BDI was developed in 1961 and was revised in 1996 to the BDI-II (Beck, Steer & Brown, 1996). It assesses depression at the levels of behaviour, emotions, cognitions, and somatic symptoms. The BDI-II consists of 21 items that are answered on a scale ranging from 0 to 3. In contrast to the CDRS-R, it allows the classification of depressive episodes into mild,
moderate, and severe. Its internal consistency has been found to range between .89 and .94 in a psychiatric sample and between .84 and .91 in a non-psychiatric sample; and test-re-test reliability and validity are high in both the original English version (Beck et al., 1996) and the German version (Hautzinger et al., 2006).

Self-rating and clinician rating instruments each have advantages and disadvantages (for an overview, see Stieglitz, 2008), and it remains unclear how similarly they assess particular symptoms of depression. A study that correlated the sum scores of the CDRS-R and the BDI-II in a healthy school sample and a clinical psychiatric population (Keller et al., 2012) found correlation coefficients of .70 and .74, respectively. Correlation between CDRS-R and BDI-II within HIV-positive adolescents in Malawi was moderately ($r = .42$, $p < .001$) (Kim et al., 2014). These instruments have not yet however been compared within a population comprising depressed adolescents only. Most of the studies that compared self-ratings and clinician ratings have focused on correlations at the level of sum scores rather than at the level of subscales or items. The one study that analysed the concordance of the self-report and structured interview versions of the Inventory for Depressive Symptomatology (Rush et al., 1986) found that items that assessed somatic aspects of depression correlated more highly than did those that assessed depressive mood (Corruble, Legrand, Zvenigorowski, Duret & Guelfi, 1999). Particularly with respect to the exploration of sensitive subjects such as suicidality, it is important for both clinicians and researchers to know how well the answers to self-administered and clinician-administered scales correlate, and whether one instrument can be replaced by the other.

Taken together, there exist many diagnostic instruments for the assessment of depressive disorders in children and adolescents, of which the BDI-II and CDRS-R are the most frequently applied in both clinical practice and research. However, the CDRS-R data do not provide information about the severity level of a depressive episode according to ICD-10, and it is unclear how much overlap there is between the information on depressive symptoms that is collected from structured interviews vs. self-report questionnaires.

### 1.4. Aetiology

The fact that depressive disorders arise in heterogeneous ways can be attributed to an interplay of multiple causes such as psychological, social and biological factors.
1.4.1. Psychological and social factors

Several psychological models have been formulated to explain the development and persistence of depressive disorders. Beck’s cognitive theory (Beck, 1976) combines the concepts of dysfunctional cognitive schemata, negative cognitive triad, and cognitive errors. Dysfunctional cognitive schemata influence the selection and interpretation of incoming data in a biased, negative way. The cognitive triad comprises a negative view about oneself, the world, and the future. Cognitive errors include over-generalization, arbitrary conclusions, and cognitive biases such as maximization (overestimation of failure and punishment) and minimization (underestimation of winning and positive reinforcement), both of which are closely connected to the reward system (Elliott, Sahakian, Herrod, Robbins & Paykel, 1997).

Seligman’s learned helplessness theory (Seligman, 1975) suggests that an individual who repeatedly experiences negative situations might come to believe that life is uncontrollable, which could lead to the development of dysfunctional cognitions such as attributing negative situations stably, internally, and globally.

According to Lewinsohn and Graf (1973), depressive symptoms arise in response to a reduction in positive reinforcements. Reasons for this reduction could include withdrawing from others, demonstrating behaviours (such as inadequate social skills) that are sanctioned rather than reinforced positively, becoming less able to enjoy positive experiences, or becoming more prone to focus on negative ones.

In addition, certain negative life circumstances such as sexual abuse, low socioeconomic status (McLeod & Shanahan, 1996), difficult family relationships and parental divorce (Gilman, Kawachi, Fitzmaurice & Buka, 2003), and non-sexual abuse or neglect (Widom, DuMont & Czaja, 2007) are risk factors for depression. In one study of depressed adolescents, 77% of participants mentioned that their depressive episodes were reactions to typical adolescent experiences such as break-ups and difficulties with parents or friends (Essau et al., 2000). In addition, chronic stress, such as that due to long-term emotional and physical neglect, is predictive for the later development of mental health symptoms (Essex, Klein & Kalin, 2002). Conversely, social supports such as caring parents are shown to be a protective factor that can prevent the occurrence of depressive disorders (Kaufman et al., 2004).
Biological factors

In summary, when it comes to the development of cognitive behavioural psychotherapies, the main elements of successful treatment consist of helping the patient learn how to recognize and alter dysfunctional cognitions, integrate positive experiences and activities into daily life, and improve the ability to handle stressors and negative life experiences. Another important factor is the involvement in the therapy process of a supportive person, such as a family member or a friend, whom the patient trusts.

1.4.2. Biological factors

The focus in this section is on neuronal aspects of depression; other biological aspects are touched on only briefly.

1.4.2.1. Genetics, sex, neurotransmitters and structural brain differences

Studies that have looked for associations between environmental aspects and genetic factors of depression have found them in 80% of cases (Dunn et al., 2011). Depressive disorders in childhood and adolescence have a genetic component, with heritability of youth-onset depression ranging from 30% to 80% (Rice, Harold & Thapar, 2002). In many cases, depression in children of depressed parents can be explained by the interplay between a short allele form of the serotonin transporter gene 5-HTTLPR and stressful life events (Eley et al., 2004). Furthermore, a significant three-way interaction in predicting depression in children has been found between 5-HTTLPR, the Met allele of brain-derived neurotropic factor, and a history of maltreatment (Kaufman et al., 2006). However, there are still studies missing that found a robust relationship between specific candidate genes or genomes and depression (Shyn et al., 2011; Sullivan et al., 2009).

Variables such as personality traits have been suggested as potential moderators on genetic influences. Some attention has been focused on the behavioural activation system, which regulates approach and appetitive motivation and is related to sensitivity of reward (Gruber et al., 2013). An altered reward system in turn has been proposed as a candidate endophenotype of depression, as it is a risk characteristic that is likely to be heritable, is present regardless of illness state, and is predictive for the onset of depression (Forbes & Dahl, 2012).

With respect to sex effects, a longitudinal study found that the risk for developing a depressive disorder after tanner stage III is higher in girls than in boys (Angold, Costello &
Brain development and development of psychiatric disorders

Worthman, 1998), which could be explained by an imbalance of androgens and oestrogens. Furthermore, one study related the cortisol awakening response (CAR; increase of cortisol levels in the first half hour after waking), of late adolescents with the subsequent development of major depressive disorder (MDD). They found that higher baseline CAR was associated with an increased risk of developing MDD highlighting the role of a dysregulated hypothalamic pituitary adrenal axis when it comes to the development of depression (Adam et al., 2010).

In a meta-analysis of structural brain abnormalities that have been associated with MDD, Bora, Harrison, Davey, Yücel & Pantelis (2012) found volume reductions in the prefrontal cortex, the anterior cingulate cortex, the caudate nucleus, and the putamen. They additionally found reports that the subgenual anterior cingulate cortex (sgACC) and the orbitofrontal cortices were smaller in patients who were being treated with antidepressants than in patients who were medication naïve. In a meta-analysis of 143 studies, Kempton et al. (2011) found that MDD is associated with larger lateral ventricles, greater volume of cerebrospinal fluid, and smaller volumes of the basal ganglia, thalamus, hippocampus, frontal lobe, orbitofrontal cortex, and gyrus rectus. In a longitudinal study of 86 adolescents without a history of depressive disorders who had been scanned during their early and mid-adolescence, Whittle et al. (2014) found that 30 subjects later experienced a depressive episode, with a relationship seen between the development of depression and volumetric changes in the hippocampus, amygdala, and putamen.

1.4.2.2. Brain development and development of psychiatric disorders

Investigating neural correlates of psychiatric disorders in a younger population can help with understanding the neurobiological origin and course of such disorders, as it avoids the confounds, that are often present in adults, such as long-term use of psychotropic medications and recurrent or chronic course of the illnesses (Cullen, 2012). Furthermore, the adolescent brain is in a state of transition in which developmental plasticity enables constant adaptation to the environment. On the one hand, such plasticity may account for the increase in several psychiatric disorders during this vulnerable period in life (Crews, He & Hodge, 2007), but on the other hand it enables the investigation of therapeutic interventions during a very sensitive phase of brain development (Davey, Yücel & Allen, 2008; Giedd et al., 2009).
Brain development and development of psychiatric disorders

Casey, Jones & Hare (2008) developed a neurobiological model that aims to explain emotional reactivity during adolescence. It highlights the interplay between relatively slowly developing brain areas, which are relevant for top-down processing (e.g., cognitive control), in comparison to relatively fast developing brain areas, which are relevant for bottom-up processing of emotional content (see Figure 1). According to this model, adolescents have functionally immature top-down regions in comparison to adults, whose systems have already matured. Consequently, the emotion-relevant system will “outperform” the relevant control system in emotional situations, which could explain increased risk-taking behaviour (e.g., use of illegal drugs or impaired driving) as well as increased development of psychopathology (e.g., affective disorders) in the vulnerable time period of adolescence.

![Figure 1 Neurobiological model demonstrating that bottom-up processes develop faster than top-down processes in adolescents (after Casey et al. 2008)](image)

Phillips, M.L., Drevets, Rauch & Lane (2003) highlighted two important neural systems for perception and regulation of emotions. The ventral system, including the amygdala and the sgACC, is relevant for identification of emotional signals and bottom-up modulation of affective states, while the dorsal system, comprising the hippocampus and prefrontal cortex, is important for the top-down regulation of emotions.
1.4.2.3. Functional differences in brain imaging in adolescents with depression

Kerestes, Davey, Stephanou, Whittle & Harrison (2014) reviewed 28 functional magnetic resonance imaging (fMRI) studies conducted in adolescents aged 13 to 18 years and in young adults aged 19 to 25 years, focusing on imaging domains such as emotion processing, cognitive control, affective cognition, reward processing, and resting-state functional connectivity. Concerning those studies, an elevated activity was found in the amygdala, the anterior cingulate cortex (ACC) (including the sgACC), and frontal brain areas such as the ventro-medial prefrontal cortex and orbitofrontal cortex. In studies that examined depression in adolescents using a reward paradigm, elevated activity in the ventral striatum was seen as well (Davey, Allen, Harrison & Yuecel, 2011; Forbes et al., 2006; Forbes et al., 2009; Forbes et al., 2010; Olino et al., 2011; Shad, Bidesi, Chen, Ernst & Rao, 2011).

In the following those brain regions will be considered more closely: when depressed patients are compared with healthy controls, altered activity in the amygdala is seen in both adults (Almeida, Versace, Hassel, Kupfer & Phillips, 2010; Arnone et al., 2012; Fu et al., 2004; Godlewska, Norbury, Selvaraj, Cowen & Harmer, 2012; Mingtian et al., 2012; Rosenblau et al., 2012; Sheline et al., 2001) and adolescents (Roberson-Nay et al., 2006; Yang et al., 2010). Several studies in adults have identified increased signal activity in the sgACC in depressed patients in comparison to healthy controls (Baeken et al., 2010; Gotlib et al., 2005; Kumari et al., 2003); and Liotti et al. (2000) showed that the generation of sadness in healthy women by reading autobiographical memory scripts, led to a heightened signal activity in the sgACC. Yang et al. (2009) found an elevated neural signal in the sgACC in depressed adolescents in comparison to a healthy control group during the performance of a stop signal task. Other researchers have found increased connectivity between the sgACC and the dorsomedial/dorsolateral frontal cortex (Davey, Harrison, Yuecel & Allen, 2012) as well as elevated activity between the sgACC and the insula/amygdala (Connolly et al., 2013). Masten et al. (2011) examined the relationship between sgACC activity during peer rejection and subsequent increases in depressive symptoms, and found that a heightened activity in sgACC during the exclusion phase was associated with elevated depression scores a year later. Furthermore, depressed adolescents, in comparison to healthy controls, demonstrated a decreased neural signal in the right hippocampus during a motivated attention task (Chantiluke et al., 2012) and an increased signal during an emotional picture task (R. Tao et al., 2012).
In sum, several biological factors including genes, sex, neurotransmitters, and structural brain differences have been identified to contribute to the development of depressive disorders. Investigating neural correlates of psychiatric disorders and their treatment early in life is of great interest; first, because elevated levels of neuroplasticity might enable rapid changes in response to treatment, and second, because the adolescent brain is not yet affected by factors such as long-term pharmacological treatment or a chronic course of the disorder, as is often the case with adults. Neurobiological models explain the increasing incidence of affective disorders in adolescents by the fast maturation of brain areas that are relevant with respect to bottom-up processes, such as the amygdala and sgACC, in contrast to slowly maturing top-down processes involving brain areas such as the hippocampus and prefrontal cortex. Those brain areas also showed altered activity in comparisons between healthy and depressed adolescents.

1.5. Pharmacological and psychotherapeutic treatment of depression in adolescents

1.5.1. Guidelines for the treatment of depression in minors

In Germany, the guidelines for the treatment of depression in adults (Deutsche Gesellschaft für Psychiatrie Psychotherapie und Nervenheilkunde, 2009) state that patients with mild to moderate depression should receive either psychotherapy or pharmacological treatment, while those with severe depression should be treated with a combination of both (level of recommendation is “A”, meaning that the recommendation is based on knowledge derived from either a meta-analysis, a systematic review including RCTs, or an RCT). With respect to the German guidelines for the treatment of depression in children and adolescents issued by the “Deutsche Gesellschaft für Kinder- und Jugendpsychiatrie Psychosomatik und Psychotherapie” (2013) older children and adolescents should be treated with either psychotherapy, the antidepressant drug fluoxetine, or a combination of both. Due to possible negative side effects of drug treatment, psychotherapy should be favoured (level of recommendation: B). In case of mild to moderate depressive symptoms, psychotherapy should be the first-line treatment, and in case of severely depressive symptoms, a combination of psychotherapeutic and pharmacological treatment should be applied (level of recommendation: consensus).
1.5.2. Efficacy of psychotherapeutic treatment

Earlier meta-analyses that compared cognitive behavioural therapy (CBT) with control treatments such as relaxation training found large effect sizes in favour of CBT (Harrington, Whittaker, Shoebridge & Campbell, 1998; Lewinsohn & Clarke, 1999; Reinecke, Ryan & DuBois, 1998). More recent meta-analyses, which applied firmer inclusion criteria, have found effect sizes ranging from small to large. Nine meta-analyses that have been published since 2000, seven of which included both children and adolescents and two of which included adolescents only, are summarized in Table 2. The mean number of included studies per meta-analysis was 20.55 (SD=9.15), and all included only studies in which a psychotherapeutic intervention, usually CBT or interpersonal psychotherapy (IPT), was compared to an active, inactive, or wait list control group. For those that reported effect sizes, the mean effect size was 0.58 (SD=.30) (Erford et al., 2011; Klein, Jacobs & Reinecke, 2007; McDermut, Miller & Brown, 2001; Michael & Crowley, 2002; Weisz, McCarty & Valeri, 2006).

1.6. Treatment programs for depression

Many of the manualized CBT programs that have been conceptualized for children and adolescents are concerned with the prevention of depression (Essau & Conradt, 2003; Horn, 2004; Poessel & Horn, 2004; Shochet, Holland & Whitefield, 1997) rather than its treatment. The following section focuses on 1) just those programs concerned with treatment, and 2) different types of CBT and of Interpersonal Psychotherapy for Depressed Adolescents (IPT-A) treatments, as both these formats have been shown to be effective (level of recommendation B).
Table 2 Meta-analyses about the efficacy of psychotherapies of depressed children and adolescents

<table>
<thead>
<tr>
<th>Author</th>
<th>Population</th>
<th>Intervention group</th>
<th>Control group</th>
<th>Effect sizes</th>
<th>Number of studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erford et al. (2011)</td>
<td>Children &amp; adolescents</td>
<td>Counselling/ Psychotherapy</td>
<td>TAU</td>
<td>0.29</td>
<td>18</td>
</tr>
<tr>
<td>David-Ferdon et al. (2008)</td>
<td>Adolescents</td>
<td>CBT/IPT</td>
<td>Waiting; TAU</td>
<td>Small to large</td>
<td>18</td>
</tr>
<tr>
<td>Spielmans, Pasek &amp; McFall (2007)</td>
<td>Children &amp; adolescents</td>
<td>Bona fide treatment</td>
<td>No bona fide treatment</td>
<td>Moderate</td>
<td>34</td>
</tr>
<tr>
<td>Klein et al. (2007)</td>
<td>Adolescents</td>
<td>CBT</td>
<td>Waiting; active control</td>
<td>0.53</td>
<td>11</td>
</tr>
<tr>
<td>Weisz et al. (2006)</td>
<td>Children &amp; adolescents</td>
<td>CBT + other treatments</td>
<td>Waiting; attention placebo; no treatment; active control</td>
<td>0.34</td>
<td>35</td>
</tr>
<tr>
<td>Compton et al. (2004)</td>
<td>Children &amp; adolescents</td>
<td>CBT</td>
<td>Active and inactive control</td>
<td>Moderate to large</td>
<td>12</td>
</tr>
<tr>
<td>Michael &amp; Crowley (2002)</td>
<td>Children &amp; adolescents</td>
<td>Psychosocial treatment</td>
<td>Waiting; attention-placebo; no treatment</td>
<td>0.72</td>
<td>15</td>
</tr>
<tr>
<td>McDermut et al. (2001)</td>
<td>Children &amp; adolescents</td>
<td>Group therapy</td>
<td>No treatment</td>
<td>1.03</td>
<td>15</td>
</tr>
</tbody>
</table>

Note: CBT=cognitive behavioural psychotherapy; IPT=interpersonal psychotherapy; TAU=treatment as usual; RR=relative risk

Overall, both CBT and IPT were shown to be effective, with moderate effect sizes on average and the German guidelines for the treatment of depression in adolescents favour psychotherapeutic treatment over drug treatment for reasons of possible side effects.

1.6.1. Individual treatment programs available in English-speaking countries

In the following section, four individual programs that are applied internationally for the treatment of depression in adolescents, all of which last between 8 and 16 sessions \((M=11; SD=3.83 \text{ sessions})\), will be described. One of the first CBT treatment programs was developed by Beck, Rush, Shaw and Emery (1979). It comprises 16 sessions that include psycho-education, restructuring of dysfunctional cognitions, problem solving, affect regulation, social skills, and involvement of parents. In an RCT with 107 adolescents who were assigned
Individual treatment programs available in English-speaking countries

to either individual CBT, nondirective supportive therapy, or systemic behaviour family therapy, CBT was found to be more effective than the other active control interventions (Brent et al., 1997).

A CBT program called Primary and Secondary Control Enhancement Training (PASCET) comprises eight sessions of 50 minutes each (Weisz, Thurber, Sweeney, Proffitt & LeGagnoux, 1997). PASCET was built on the two-process model of perceived control and coping: primary control involves coping by making objective conditions fit one’s wishes (e.g., peer relationships), while secondary control involves coping by adapting oneself to conditions that cannot be altered. Weisz et al. (2009) randomly assigned 57 children and adolescents aged 8 to 15 years to either PASCET or treatment as usual (TAU). Participants in both groups improved significantly, but there was no difference in improvement between the groups. However, compared with TAU, subjects in the PASCET group needed fewer sessions to reach levels of recovery and were less likely to require additional services; also, sessions were less costly.

Vostanis and Harrington (1994) developed an individual treatment program consisting of eight 45-minute sessions. The aims of this program are to help children and adolescents to improve their recognition and naming of different emotions, to change negative cognitions, and to extend social skills. Efficacy was investigated in two studies. Vostanis, Feehan, Grattan & Bickerton (1996) compared CBT with a non-focused intervention in 56 children. At the end of the treatment (average of six sessions), 87% of the CBT group and 75% of the control group no longer fulfilled criteria for a depressive disorder, with no superiority of CBT over the non-focused intervention. Wood, Harrington and Moore (1996) randomly assigned outpatients aged 9 to 17 years to either the depression treatment program or relaxation training. A total of 48 participants completed the trial. The treatment group was significantly more likely to improve than the control group, with a moderate effect size of .73. These results were only found in the patient ratings, and did not reach significance in the parental ratings.

IPT-A is a brief, specified psychotherapy that can be applied in either a group or an individual setting. It lasts for 12 weeks, and addresses common adolescent developmental issues such as separation from parents, interpersonal relationships, and peer pressure. To test efficacy of the treatment, Mufson, Weissman, Moreau and Garfinkel (1999) randomly assigned 24 participants to an IPT-A treatment group and 24 to a clinical monitoring group.
International group treatment programs

Significant group differences were found post-treatment in favour of the treatment group. In a further study, Mufson, Pollack, Olfson, Weissman and Hoagwood (2004) investigated whether IPT-A would be effective in a school-based mental health setting, by randomly assigning 63 depressed students to either IPT-A or TAU delivered by school-based health clinicians. Results indicated that participants treated with IPT-A showed greater symptom reduction compared to those who received TAU. Tang, Jou, Ko, Huang and Yen (2009) randomly assigned 73 depressed adolescents aged 12 to 18 years to either IPT-A or TAU, and found significantly higher reduction of depression scores in the IPT-A group.

In another study, IPT-A and CBT were compared with each other and with a wait list group (WL) (Rossello & Bernal, 1999). The CBT program was based on the cognitive-behavioural model developed by Muñoz and Miranda (1986), which was originally developed as a group intervention for adults and was adapted for the individual treatment of adolescents. It consists of 12 one-hour individual therapy sessions, and is based on the concepts of cognitive behavioural therapy and rational-emotive therapy, aiming to identify thoughts and actions that influence depressive feelings. Results of the study that compared IPT-A, CBT, and WL indicated that both active treatment forms led to significantly reduced depressive symptoms when compared to the WL condition, but there were no differences on depression scores between IPT and CBT.

Taken together CBT was shown to be superior to active control treatment in two studies and comparable to TAU in two further studies. Also IPT-A was shown to be superior to clinical monitoring and TAU in two studies.

1.6.2. International group treatment programs

In a review of the efficacy of group cognitive behavioural therapy (CBT-G) for the treatment of unipolar depressive disorder in adults, Oei and Dingle (2008) reported small ($d=0.1$) to large ($d=2.87$) effect sizes, with a mean effect size of $d=1.1$. In a review of CBT-G versus individual CBT, McDermut, Miller and Brown (2001) found a comparable mean effect size of $d=1.02$ (average effect size of 1.27 for CBT-G; 1.49 for individual CBT). The difference was not significant, indicating that CBT-G is comparable to individual CBT. As CBT-G can be delivered to multiple participants with a minimum amount of time and staff, it offers advantages with respect to both research and treatment (Oei & Dingle, 2008).
Besides of the treatment program we developed (see section 1.6.5) there existed three programs for the treatment of depressed children and adolescents between the ages of 8 and 21 years in the German language; two of which are conceptualized for group therapy and one for individual therapy (see Table 3). The number of sessions in these programs ranges from 8 to 17 ($M=11.66; SD=4.73$), while the session durations range from 45 to 100 minutes ($M=78.33; SD=29.30$). Both of the group therapy programs are derived from the English-language program “Coping with depression course for adolescents” (CWD-A). One of them, titled “Stimmungsprobleme bewältigen” (Dealing with mood problems), focuses on psycho-education, relaxation, cognitive restructuring, problem-solving, and social skills (Ihle & Herrle, 2011). The other, “Kognitive Verhaltenstherapie bei Kindern und Jugendlichen” (Cognitive behavioral therapy in children and adolescents) (Abel & Hautzinger, 2013) focuses on psycho-education, positive activation, cognitive restructuring, social skills, and parent sessions. The third program, which provides individual treatment, is derived from the program developed by Vostanis and Harrington (1994) (see section 1.6.1) and was translated into German by Jans, Warnke, and Remschmidt (Harrington, 2001).

None of these three German-adapted programs has been evaluated in an RCT. Pilot studies were conducted on the “Stimmungsprobleme bewältigen” program, with the results summarized by Straub, Keller, Sproeber, Koelch und Plener (2014). The “Kognitive Verhaltenstherapie bei Kindern und Jugendlichen” (Harrington, 2001) program was evaluated in a pre-post-follow-up test design that enrolled 33 depressed adolescent in- and outpatients. Results indicated a significant reduction of depressive symptoms in the pre-post-test comparison, based on both self-ratings and parent ratings, with medium to large effect sizes, and the results were still robust at a follow-up test six months later. The individual program has only been evaluated in the English-language studies described above (see Section 1.6.1).
1.6.4. Duration of treatment

The duration of therapeutic treatment plays an important role when it comes to conceptualization of psychotherapy, and is also of interest from an economic point of view. Two models of the dose-effect relationship of psychotherapeutic treatment exist. In the *good enough level model*, Barkham et al. (2006; 1996) found session-to-session improvement to be more or less linear, assuming that symptoms improve until the patient reaches a *good enough level*, at which point the patient and/or therapist stops treatment or focuses on other psychotherapeutic aims. The *model of negative acceleration* (Howard, Kopta, Krause & Orlinsky, 1986) states that symptom improvement after psychotherapeutic treatment is a negatively accelerated function of treatment length, in which 30% of patients improve after two sessions, 41% after four sessions, 53% after eight sessions, 63% after 13 sessions, and 83% after 52 sessions. Lambert, Hansen, and Finch (2001) found that 50% of patients showed significant symptom reduction after only 7 sessions and 75% after 14 sessions. Supporting the negative acceleration model, Barkham et al. (1996) randomly assigned depressed patients to either 8 or 16 sessions of time-limited psychotherapy (CBT or IPT). For most of the outcome parameters, the eight-session group showed greater symptom reduction at the end of treatment (after eight sessions) than did patients in the 16-session group at mid-treatment (after eighth session). It seems that symptom change occurs faster when tighter time restrictions are imposed. Supporting the model of negative acceleration, the meta-analytic review of Harrington et al. (1998) demonstrated that a quarter of depressed adolescents remit following relatively short psychosocial interventions of 8 to 12 weekly sessions, while Goodyer et al. (2007) showed that 21% of adolescents with

### Table 3 German-language therapy programs for the treatment of depressed minors

<table>
<thead>
<tr>
<th>German version of English</th>
<th>Original Age range</th>
<th>Setting</th>
<th>Number and duration of sessions</th>
</tr>
</thead>
<tbody>
<tr>
<td>„Kognitive Verhaltenstherapie bei depressiven Kindern und Jugendlichen“</td>
<td>8-17 years</td>
<td>Individual setting</td>
<td>8 sessions of 45 minutes each</td>
</tr>
<tr>
<td>„Stimmungsprobleme bewältigen“</td>
<td>16-21 years</td>
<td>Group setting</td>
<td>10 sessions of 90 minutes each</td>
</tr>
<tr>
<td>„Kognitive Verhaltenstherapie bei Kindern und Jugendlichen“</td>
<td>12-18 years</td>
<td>Group setting</td>
<td>17 sessions of 90–120 minutes each</td>
</tr>
</tbody>
</table>
Development of a brief CBT-G called MICHI

Moderate to severe depressive symptoms improve after a brief psychosocial intervention (M=3 sessions). In a recent meta-regression analysis Cuijpers, Huibers, Ebert and Koole (2013) looked at the relationship between number of sessions, frequency, and intensity of depression therapy and treatment efficacy in adults. They found that the number of weekly sessions rather than duration of treatment was associated with larger effect sizes. An increase from one to two sessions per week increased the effect size, with g=.45. Those findings highlight the advantages of interventions that are brief and intensive.

In summary, the good enough level model assumes a linear relationship between sessions and treatment response, while the negative acceleration model assumes greater improvement within earlier over later sessions which was supported by several studies. To our knowledge, there exists no treatment program that combines the potential advantages of all the following: 1) based on CBT, 2) brief, 3) intense, 4) delivered via group therapy and 5) for all severities of depression. Furthermore, none of the programs available in Germany for the treatment of depression in adolescents has been evaluated with respect to efficacy by means of an RCT. The program described in the following section was designed to address all of these issues.

1.6.5. Development of a brief CBT-G called MICHI

Based on what we viewed as gaps in the treatment options currently available, we developed a program titled MICHI, which stands for “Manualized Intervention to Cope with depressive symptoms, Help strengthen resources and Improve emotion regulation” (Sproeber, Straub, Fegert & Koelch, 2012). MICHI encompasses five weekly sessions of approximately 75 minutes each, plus one booster session that is held five weeks after the last regular session. Participants are depressed adolescents between 13 and 18 years of age. Four to six participants are enrolled in a group, which is led by two trainers. Patients receive a handout at each session, and trainers are provided with a manual to ensure adherence to the procedures. Contents of the sessions include psycho-education, behavioural activation, cognitive restructuring, enhancement of self-esteem, skills for improved problem solving, and emotion regulation. Participants are asked to bring a trusted person (e.g., parent, sibling, or friend) to the fifth session in order for this individual to be trained on how to help the patient to prevent relapse. Unlike other programs, MICHI also teaches skills on how to deal with acute crises such as elevated levels of suicidal ideation. Furthermore, it is the only
Neural correlates of depression treatment

program available in Germany for the treatment of depression in adolescents that has been tested in two pilot studies as well as in an RCT (see Section 3.6 to 3.8).

1.7. Neural correlates of depression treatment

RCTs looking at evaluating treatment efficacy have traditionally assessed improvements in depressive symptoms, using questionnaires or structured interviews. New approaches in research are additionally evaluating treatment effects by assessing altered neuronal activity and attempting to identify biomarkers for illness severity and improvement as well.

1.7.1. Neural correlates of pharmacological treatment

A wide range of studies has shown activity levels in the amygdala, the subgenual parts of the ACC, the hippocampus, and the prefrontal cortex to be elevated in depressed individuals in comparison to healthy controls (see Section 1.4.2.3). Several studies have found (Rosenblau et al., 2012) elevated activity in the amygdala of depressed adults to normalize (Godlewska et al., 2012) and to match that of a healthy control group (Rosenblau et al., 2012; Sheline, 2000) following treatment with antidepressants. Similarly, a significant reduction of sgACC activity was seen after six weeks of paroxetine (Kennedy et al., 2001) or eight weeks of fluoxetine (Mayberg et al., 2000); a significant reduction of hippocampal activity was seen after six weeks of paroxetine (Kennedy et al., 2001) and eight weeks of fluoxetine (Fu et al., 2007); and other studies have found altered activity in the prefrontal cortex following treatment with medication (Goldapple et al., 2004; H. Tao et al., 2013).

1.7.2. Neural correlates of psychotherapeutic treatment

To date, ten neuroimaging studies have investigated neural changes before and after psychotherapeutic treatment in depressed adults, using active paradigms, involving either processing emotional stimuli, cognitive control, or processing of reward, or resting state (see Table 4). However, there have been no studies investigating neural correlates of psychotherapy of depression in adolescents.
# Neural correlates of psychotherapeutic treatment

## Table 4 Studies investigating neural correlates of psychotherapeutic treatment of depression by means of an active paradigm

<table>
<thead>
<tr>
<th>Author</th>
<th>Participants</th>
<th>Paradigm</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crowther et al. (2015)</td>
<td>23 depressed adults: before and after 12 weekly sessions of CBT-G, 20 healthy controls: before and after equivalent period of time</td>
<td>Resting state</td>
<td>Response to psychotherapy in depressed adults was predicted by pretreatment connectivity of the right insula with the right middle temporal gyrus and left intraparietal sulcus with the orbital frontal cortex.</td>
</tr>
<tr>
<td>Yoshimura et al. (2014)</td>
<td>23 depressed adults: before and after 12 weekly sessions of CBT-G, 15 healthy controls: before and after equivalent period of time</td>
<td>fMRI, emotional word processing task</td>
<td>Following CBT, activity in the medial prefrontal cortex and vACC was increased for positive stimuli and decreased for negative stimuli.</td>
</tr>
<tr>
<td>Buchheim et al. (2012)</td>
<td>16 depressed adults: before and after 15 months of psychodynamic intervention, 17 healthy controls: before and after equivalent period of time</td>
<td>fMRI, presentation of attachment-related scenes</td>
<td>Patients showed a higher activation in the left anterior hippocampus, amygdala, subgenual cingulate, and medial prefrontal cortex before treatment, and showed reduction in these areas after 15 months. Symptom reduction was associated with activity change in the prefrontal cortex.</td>
</tr>
<tr>
<td>Ritchey, Dolcos, Eddington, Strauman &amp; Cabeza (2011)</td>
<td>11 depressed adults: before and after CBT, 7 healthy controls: before and after equivalent period of time</td>
<td>fMRI, emotional picture task</td>
<td>In the patients, post-treatment increases in ventromedial prefrontal cortex activation were seen, along with enhanced arousal in the amygdala, caudate, and hippocampus.</td>
</tr>
<tr>
<td>Dichter et al. (2010)</td>
<td>12 depressed adults: before and after BAT, 15 healthy controls before and after equivalent period of time</td>
<td>fMRI, cognitive control task</td>
<td>Psychotherapy resulted in decreased activation in response to cognitive control stimuli presented within a sad context in the paracingulate gyrus, right orbital frontal cortex, and right frontal pole. The strength of pretreatment activation in the paracingulate gyrus predicted the strength of symptom change.</td>
</tr>
<tr>
<td>Dichter et al. (2009)</td>
<td>12 depressed adults: before and after BAT, 15 healthy controls before and after equivalent period of time</td>
<td>fMRI, reward paradigm</td>
<td>Relative to the control group, patients who received psychotherapeutic treatment showed altered activity in the paracingulate gyrus and the right caudate nucleus during reward anticipation, and altered activity in the paracingulate and the orbitofrontal gyri during reward feedback.</td>
</tr>
<tr>
<td>Fu et al. (2008)</td>
<td>16 depressed adults: before and after 16 sessions of CBT, 16 healthy controls: before and after equivalent period of time</td>
<td>fMRI, affect recognition task</td>
<td>A significant interaction effect of group by time was found for the right amygdala, the hippocampus, and the anterior cingulate.</td>
</tr>
</tbody>
</table>
Neural correlates of psychotherapeutic treatment

Patients with the lowest linear load response in the anterior cingulate at baseline were those with the greatest clinical response.

Goldapple et al. (2004) 14 depressed adults: before and after 26 weeks of CBT PET Pre-post increase in metabolic activity within the hippocampus and the dorsal cingulate cortex.

Pre-post decreases in the dorsolateral and ventrolateral prefrontal regions, orbital frontal regions, posterior cingulate, inferior parietal regions, and inferior temporal regions.

Martin, Martin, Rai, Richard-son & Royall (2001) 13 depressed adults: before and after a 6-week course of one-hour weekly sessions of IPT SPECT Post-treatment increase of blood flow in the right posterior cingulate cortex and the right basal ganglia.

Brody et al. (2001) 24 depressed adults: before and after 12 weeks of IPT PET The IPT group showed decreased metabolism in the right prefrontal cortex and left anterior cingulate gyrus, and increased metabolism in the left temporal lobe metabolism.

16 healthy control: before and after equivalent period of time

Abbreviations: fMRI= functional Magnetic Resonance Imaging; CBT=cognitive behavioural therapy; CBT-G=cognitive behavioural therapy in a group setting; BAT=behavioural activation therapy; vACC=ventral anterior cingulate cortex; PET= positron emission tomography; SPECT= single-photon emission computed tomography

In an investigation of the relationship between neural activity changes and symptom improvement, Siegle, Carter and Thase (2006) found that activity in the sgACC of depressed adults explained 56.7% of the variance of the pre-test depression scores. Logistic regression demonstrated that sgACC activity prior to CBT explained subsequent remission after treatment in seven of nine patients. Konarski et al. (2009) found that in contrast to responders, non-responders to CBT exhibited pre-treatment hypermetabolism at the interface of the pregenual and subgenual ACC. In contrast to that finding, Yoshimura et al. (2013) found that improvement of depressive symptoms was negatively related to vACC signal change during processing of negative stimuli.

In sum, the amygdala, hippocampus, anterior cingulate cortex, and prefrontal cortex have repeatedly been shown to be associated with responses to both psychotherapeutic and pharmacological treatment, and activity in the sgACC has been shown to be related to subsequent treatment response.
Neural correlates of depression treatment in children and adolescents

1.7.3. Neural correlates of depression treatment in children and adolescents

To date, only one study has examined the effects of therapy and a further study the effects of medical treatment on depression-relevant brain areas in children and adolescents. Forbes et al. (2010) examined reward-related brain functioning in adolescents with depression before (but not after) treatment with either CBT alone or CBT plus SSRI. Pre-treatment striatal activity was associated to symptom improvement in both forms of treatment. Tao et al. (2012) compared brain activation prior to and after eight weeks of treatment with fluoxetine, and found that formerly elevated activity levels in the sgACC and amygdala normalized to levels of a healthy control group after treatment.

Taken together all of the psychotherapeutic studies and most of the pharmacological studies have been done in adults and no controlled study has investigated psychotherapeutic effects on neural substrates of depression in children and adolescents.

1.7.4. Paradigm for assessing neuronal correlates of depression treatment

Depressive symptomatology has been found to be associated with dysfunctional reward processing, and may therefore be attributed to the same underlying neural mechanisms (Forbes & Dahl, 2005; Olino et al., 2013). Some brain areas, such as the amygdala, are relevant for both the processing of emotions and reward (Gabriel, Burhans & Kashef, 2003). Deep brain stimulation to the sgACC, a brain region involved in reward processing, has been shown to help adults with severe chronic depression (Schlaepfer et al., 2008). Furthermore, pre-CBT activation of the ventral striatum by means of a reward task was shown to predict symptom improvement after therapy in adolescents (Forbes et al., 2010). The hippocampus has also been reliably shown in animal, lesion, and imaging studies to be important with respect to processing of rewards (Haber & Knutson, 2010).

Reward paradigms have been demonstrated to be suitable for investigating depressive symptoms in adolescents, but have rarely been investigated for the assessment of psychotherapeutic treatment effects. The paradigm we chose for assessing the effects of CBT was a monetary incentive task, which can be used irrespective of cultural and social background and with a good test-re-test reliability (Abler, Hahlbrock, Unrath, Groen & Kassubek, 2009).
Aims and research questions of the present work

2. Aims and research questions of the present work

As described in Section 1, compared to the literature for the adult population, there is limited understanding about depressive disorders in minors with respect to prevalence, diagnostic standards for the assessment of symptoms, efficacy of psychotherapy treatments, and underlying neural correlates of treatment effects. This thesis aims to close some of these gaps.

While the prevalence rate of depressive disorders in minors has remained fairly constant, the number of antidepressant prescriptions and the number of individuals receiving outpatient treatment for depression have been increasing (Annuss et al., 2010; Zito et al., 2003). So far, there is a lack of recent studies that assessed whether the number of depressed adolescent patients referred for inpatient treatment has increased within the last years. To analyse trends of referrals for inpatient treatment, we looked at the number of F3 diagnoses (the ICD-10 classification of affective disorders) that were collected from children and adolescents who were admitted for inpatient treatment in Germany between the years 2003 and 2012.

A frequent reason for referral to inpatient treatment for a depressive disorder is that this disorder is often accompanied by additional problems such as missing school and elevated levels of suicidal ideation and planning (Mehler-Wex, 2012). Diagnoses classified as F3 include not only depression but also bipolar disorders, which have been shown to be highly associated with elevated levels of suicidality (Allison et al., 2001). However, to our knowledge, no previous study has looked at whether symptoms of mania apart from those of depression predict symptoms of suicidality in adolescents.

The most frequently used instruments for diagnosing depression, and in doing so also the symptom of suicidality, are the CDRS-R and the BDI-II (Mayes et al., 2010; Subica et al., 2014). Some international RCTs on depressed adolescents have restricted enrolment to subjects with a CDRS-R score >45 (Treatment for Adolescents With Depression Study Team, 2007), which indicates a severity level of moderate to severe. In our treatment study, to avoid a positive bias, we wished to include subjects with mild depression as well. No study has yet assessed which level of severity of depression, as diagnosed using ICD-10, corresponds to which score on the German version of the CDRS-R. However, according to the work of Guo et al. (2006), who based their ratings on clinical estimations rather than
Aims and research questions of the present work

structured interviews, a total score between 30 and 40 on the English version of the CDRS-R indicates depression of mild severity.

According to the German guidelines, questionnaires can be used as screening tools, and a diagnosis should then be verified by means of a structured interview (Deutsche Gesellschaft für Kinder- und Jugendpsychiatrie Psychosomatik und Psychotherapie, 2013). However, there is a lack of knowledge of how similarly these two types of instruments measure the construct of depression in minors. Previous studies found high correlations at the sum score level, but no studies have compared ratings at the subscale and item levels. To address this, we compared the BDI-II and CDRS-R on all three levels.

Diagnostic instruments are necessary for validly and reliably detecting depressive symptoms and determining their severity, so that, depending on the severity level of depression, suitable treatment options can then be recommended. According to the German guidelines for depression treatment in minors, psychotherapeutic interventions, specifically CBT and IPT, are recommended for the treatment of depressive episodes of mild or moderate severity, and a combination of pharmacological and psychotherapeutic interventions is recommended for the treatment of severe episodes. Further, previous studies have shown that interventions that are brief and that are applied in a group setting can be effective. A literature search revealed that the therapy program options available in the German mental health system for the treatment of depression in adolescents do not include any that possess all the following features: 1) brief, 2) based on CBT, 3) provided as group therapy, 4) directed at patients with any severity of depression, and 5) had been evaluated in an RCT.

Those considerations led to the development of MICH, described in Section 1.6.5. This program integrates the advantages named above. An important aspect to keep in mind in the development of new treatment programs is that some studies have found that suicidal ideation may initially increase during psychotherapeutic treatment, especially in adolescents and young adults (Simon & Savarino, 2007); thus, it is important to first evaluate a new program in the protected environment of an inpatient setting before evaluating it in the outpatient setting. Therefore, the first pilot study was conducted with inpatients, and focused on determining feasibility, acceptance, and first trends of efficacy concerning depression scores and effects on suicidality. In a next step, we conducted a second pilot study in outpatients, using feedback from the first set of participants and trainers to re-work
Aims and research questions of the present work

some aspects of the therapy program. In a further step, the efficacy of the program was assessed in an RCT in which depressed adolescent outpatients were randomly assigned to either an intervention group that received MICHI or to a waiting control group that received TAU.

Responses to both psychotherapeutic and pharmacological treatment have been repeatedly shown to be associated with activity changes in the amygdala, hippocampus, ACC, and prefrontal cortex; and activity in the sgACC has been shown to be related to subsequent treatment response. However, no study to date had investigated neural correlates in adolescents of pre-to-post psychotherapeutic treatment in comparison to pre-to-post TAU.

Summary of minor hypotheses with respect to new insights on epidemiology, symptoms, and diagnostic instruments of depression in adolescents:

**H1:** It was expected that the number of children and adolescents being referred for inpatient treatment due to a diagnosis of depressive disorder has increased over a time period of ten years (1st scientific article of Plener, Straub, Fegert & Keller, 2015).

**H2:** It was expected that both suicidal ideation and behaviour are predicted by mania symptoms, above the symptoms of depression (2nd scientific article of Straub, Keller, Sproeber, Koelch & Plener, 2015).

**H3:** It was expected that a total CDRS-R score of between 30 and 40 would indicate depression of mild severity (3rd scientific article of Plener, Grieb, Sproeber, Straub, Schneider, Keller & Koelch, 2012).

**H4:** It was expected that a high correlation would be found between the CDRS-R and the BDI-II at the sum score level. With respect to the subscale level, it was expected that higher correlations would be found between those subscales that assess more objective aspects of depression (e.g., somatic aspects) than between those that assess subjective aspects (e.g., depressive mood); while at the item level, it was expected that the highest correlations would be found between...
Aims and research questions of the present work

those items that assess similar rather than divergent aspects of depression (4th scientific article of Straub, Plener, Koelch, & Keller, 2014).

Summary of major aims and hypothesis with respect to feasibility, efficacy and neuronal correlates of the MICHI program:

Before developing a new therapy program, it is necessary to have a full understanding of existing therapy programs and their appropriate effectiveness and efficacy.

**Aim:** To review current literature on cognitive behavioural and interpersonal group therapy programs for the treatment of depression in adolescents, and to summarize the results of studies (5th scientific article of Straub, Nicolaus, Plener, Sproeber & Koelch, 2014).

**H5:** In a pilot study with depressed adolescent inpatients, it was expected that MICHI would be found to be feasible, accepted, and to reveal first trends of efficacy (6th scientific article of Straub, Koelch, Fegert, Plener, Gonzalez-Aracil, Voit & Sproeber, 2013).

**H6:** In a pilot study with depressed adolescent outpatients, it was expected that MICHI would be found to be feasible, accepted, and to reveal trends of efficacy (7th scientific article of Straub, Sproeber, Plener, Fegert, Bonenberger & Koelch, 2014).

**H7:** It was expected that a significant interaction effect would be seen between time points of measurement (pre/post) and group (patients who received MICHI vs. patients in the wait-list control group who received TAU), with a greater improvement in symptoms seen in the intervention group (8th scientific article of Straub, Plener, Keller, Fegert, Sproeber & Koelch, accepted).
Aims and research questions of the present work

**H8:** It was expected that symptom changes in the MICHI group would be accompanied by activity changes in depression-relevant brain areas such as the amygdala, sgACC, hippocampus and frontal cortex which would not be seen in the TAU group. Furthermore, it was expected that pre-treatment sgACC activity would correlate with subsequent pre-post symptom changes (9th scientific article of Straub, Plener, Sproeber, Sprenger, Koelch, Groen & Abler, 2015).
Results

3. Results

3.1. Changes in prevalence rates of ICD-10 F3 diagnoses in the inpatient setting


Introduction: Prevalence rates for depressive disorders remained stable between 1965 and 1996. However, the number of minors being treated in the outpatient setting, increased between 2005 and 2008 as did the numbers of those receiving pharmaceutical treatment. Furthermore, numbers of minors, being referred to the inpatient setting due to F3 diagnoses, increased as well between 2000 and 2007. However, there is a lack of newer studies that analysed whether numbers of F3 diagnoses are still increasing in the in- and outpatient setting.

Methods: This study analysed the prevalence of F diagnoses according to ICD-10 in minors up to 15 years of age from all German psychiatric hospitals between 2003 and 2012. Changes over the years were assessed by means of linear regression analyses.

Results: A significant increase was seen in most diagnostic groups, including affective disorders (the F3 category in ICD-10). The only diagnostic groups that showed stable or decreasing rates of hospital treatments in the ten-year time frame were organic (F0), schizophrenic (F2), and personality and behavioural disorders (F6).

Conclusion: The reasons for increasing prevalence rates might be an increased attention paid to psychiatric disorders in the general population; furthermore, higher numbers of inpatients might be traced back on shorter durations of stay in psychiatric hospitals, which in turn might be explained by improvement of treatments.

3.2. Association between symptoms of depression plus mania and suicidal behavior

Introduction: With respect to affective disorders (the F3 category in ICD-10) in minors, bipolar disorders are less prevalent than depressive disorders. However, an early onset of bipolar disorder coincides with an elevated risk for suicide. The aim of this article was to investigate whether mania symptoms, above symptoms of depression, predict suicidal ideation and attempts.

Methods: A total of 1,117 adolescents from 13 German schools (mean age = 14.83; SD=.63) completed questionnaires for the assessment of depression symptoms (Centre for Epidemiological Studies Depression Scale), mania symptoms (nine questions for the assessment of mania symptoms according to DSM-IV), and lifetime suicidal behaviour (Self-Harm Behaviour Questionnaire). Logistic regression with a block-wise entry method was applied to analyse the predictive value of mania and depression symptoms on suicidal ideation and attempts.

Results: Results indicated that 39.4% of the girls and 23.1% of the boys reported lifetime suicidal thoughts; 7.1% of the girls and 3.9% of the boys reported a lifetime history of suicide attempts; 18.7% of the overall sample reported having experienced elevated symptoms of depression; and 9% reported having had elevated levels of mania symptoms during the past week. Elevated depression and mania scores were associated with lifetime suicidal ideation and suicide attempts. Regression analyses revealed that elevated levels of mania symptoms, above symptoms of depression, explained the occurrence of suicidal ideation. Furthermore, mania symptoms, above symptoms of depression and age, predicted suicide attempts.

Conclusion: It can be concluded that bipolar symptoms heighten the possibility for suicidal behaviour, which should alert clinicians.

3.3. Convergence of CDRS-R scores with a mild depressive episode according to ICD-10


Introduction: Until now, no study had related the dimensional scores of the German version of the CDRS-R to the categorical diagnoses (mild, moderate, or severe depressive episode) of the ICD-10.
Methods: Clinicians were asked to watch a videotape showing a structured interview with an adolescent girl being asked about depressive symptoms. They were split into two groups, with one group asked to rate the girl’s depressive symptoms using the CDRS-R and the other to make a clinical diagnosis by means of the ICD-10.

Results: A raw score in the CDRS-R between 35 and 40 was found to be indicative for a mild to moderate depressive episode according to ICD-10; specifically, a raw score of greater than 36 points was an indicator for a clinical diagnosis of a mild to moderate depression in nearly two-thirds of the ratings.

Conclusion: Different studies found a CDRS-R score of 40 to indicate a depressive symptomatology. Differences might be traced back on different classification systems applied (DSM-IV/5 versus ICD-10).

3.4. Agreement between BDI-II and CDRS-R in assessing depression in minors


Introduction: Previous studies have demonstrated a high concordance between a patient’s self-report of depression and the clinician’s assessment. However, few studies have focused on the concordance at the sum-score level, the subscale level, and the single-item level in a psychiatric adolescent sample. The influence of additional variables (age, sex, IQ, treatment modality) on correlational strength and on whether an individual under- or overestimates his/her symptomatology was assessed as well.

Methods: For correlational analyses, BDI-II and CDRS-R scores were collected from 105 adolescents ($M=15.94$ years; $SD=1.63$) within one week.

Results: At the sum-score level, there was a high correlation between the self-reports and the clinicians’ assessments ($r=.67$, $p<.001$). At the subscale level, contrary to previous studies, items assessing somatic contents did not have a higher concordance ($r=.53$), even if they appeared more objective, than did items assessing cognitive and affective contents ($r=.54$). At the symptom level, the correlation between items assessing similar contents was moderate to large. The highest concordance was shown for the item that assessed suicidal ideation ($r=.57$, $p<.001$). Additional variables had no influence on the strength of correlation.
Literature review on psychotherapeutic group treatment for depressed minors

between self-reports and structured interview assessments. However, self-reports that tended to overestimate symptomatology in comparison to the clinician’s rating were seen more with outpatients than with inpatients, and more with patients with a high IQ than those with a low IQ.

Conclusions: The high correlation between self-report and structured interview assessments, especially with respect to the assessment of suicidality, indicates that questionnaires can deliver first important information about symptoms of depression, comparable to asking for them directly. As the correlation between both instruments is high but not perfect, both instruments have rather complementary character but one instrument shouldn’t be replaced by the other.

3.5. Literature review on psychotherapeutic group treatment for depressed minors


Introduction: According to the German guidelines for the treatment of depression in adolescents, individuals who are mildly to moderately depressed should receive psychotherapeutic treatment, while those who are severely depressed should receive a combination of pharmaceutical and psychotherapeutic treatment. With respect to psychotherapy, guidelines recommend CBT or IPT. According to the results of a meta-analysis, effect sizes are comparable between the individual setting and the group setting.

Methods: Of 280 hits in a literature search that were reviewed for titles and abstracts, 46 full texts were read and 25 studies were finally included into the review.

Results: Most of the studies investigated the efficacy of CBT, two investigated the efficacy of IPT, and two investigated a combination of these. The duration of psychotherapeutic treatment varied from five sessions of 75–90 minutes each to 16 sessions of 90–120 minutes each. Only three studies analyzed the effectiveness of treatment programs in Germany, and two of these referred to the same population. Concerning studies that aimed to identify the efficacy of English-speaking treatment programs, 16 out of 25 studies were RCTs, and five were pilot studies. In 12 studies, the control group was a wait-list, while in four studies it was
Pilot study on feasibility and acceptance of MICHI in adolescent inpatients

TAU or an unspecific treatment. For English-language CBT group therapies, effect sizes ranged from .02 to 1.34.

**Conclusions:** In most of the studies, post-test depression scores were significantly lower in the intervention group than in the control group. However, in two studies, reduction of depression scores was comparably between the groups. In both those cases, the control group had received TAU, and it needs to be analysed in future studies whether the specific treatment is comparable or superior to TAU.

### 3.6. Pilot study on feasibility and acceptance of MICHI in adolescent inpatients


**Introduction:** In a first step, MICHI was studied with respect to feasibility and first trends of effectiveness with depressed adolescent inpatients. The inpatient setting was chosen for ethical reasons, as MICHI had not been evaluated before and because depression is frequently accompanied by elevated levels of suicidality, especially at the beginning of a treatment.

**Methods:** Nine depressed adolescent inpatients with a mean age of 16.33 years (*SD*=1.92) were enrolled. Inclusion criteria included age between 13 and 18 years, IQ score ≥85, a raw-summary score ≥36 on the CDRS-R, and a diagnosis of a mild, moderate, or severe depressive episode. Co-morbid diagnoses were allowed except for a current diagnosis of a bipolar disorder, schizophrenia, and substance abuse. Antidepressant medication was allowed, but had to be stabilised three weeks prior to the start and during participation in the program. The treatment comprised four sessions of 90 minutes each. Feasibility was assessed by means of participants’ attendance at the sessions and evaluations by the trainers. Acceptance of the training program and evaluation of its contents were assessed by means of a process evaluation questionnaire (1=not true to 5=true). One question assessed the global evaluation of the program (1=very bad to 10=very good). To assess trends of
effectiveness, the CDRS-R was assessed both before and after treatment. Suicidal ideation was assessed by means of Item 13 of the CDRS-R.

**Results:** With respect to feasibility, the overall attendance rate was fair. The trainers stated that the treatment manual was well-structured but that sessions were too long to guarantee fully concentrated participation. With respect to contents, participants rated “emergency plan for acute crises” as being the most helpful and “relaxation techniques” as being the least helpful. The global evaluation revealed that participants rated MICHI as being positive and effective overall ($M=7.22; SD=1.79$). Pre-post-test comparisons delivered a significant reduction of CDRS-R depressive scores ($z=-2.66; p=.008$) and suicidality.

**Discussion:** Attendance was fair, but could be improved by the establishment of a reinforcement system in future groups. In a further step, the treatment manual was reworked, sessions were shortened to 75 minutes, and the contents of sessions were reorganised, resulting in a final number of five regular sessions. The content on “relaxation techniques” was removed from the program. The improvements seen with respect to depressive scores and suicidality were promising, and were comparable with the results of other studies. The findings were limited with respect to the small number of participants and to the facts that some patients were receiving medication, that the inpatient setting could influence results as well, and that no randomized controlled trial was applied.

**3.7. Pilot study on feasibility and acceptance of MICHI in adolescent outpatients**


**Introduction:** Before evaluating MICHI in a randomized controlled trial, we decided to evaluate its feasibility and preliminary data on effectiveness in a second pilot study, this time with outpatients. This was done for several reasons. First, the contents of the treatment program had been reordered following comments of the trainers in the first pilot study, ending up with fewer sessions and some content deleted. Second, having demonstrated fair attendance in the inpatient setting, we wanted to test whether the same would be true in
RCT for the assessment of efficacy of MICHI in depressed adolescent outpatients

the outpatient setting. Third, as we were including individuals who were diagnosed with a severe depressive episode, which is associated with a lowered psychosocial functioning level, we wanted to test whether it would be feasible to apply MICHI in an outpatient setting as well.

**Methods:** Fifteen outpatients (11 females) with a mean age of 16.42 years ($SD=1.43$) were enrolled. Inclusion and exclusion criteria were the same as in the first pilot study (see Section 3.6). MICHI comprised five regular sessions and one booster session, each lasting between 75 and 90 minutes. Feasibility of the program was assessed by means of attendance rate, participants’ and trainers’ feedback, and fidelity of implementation. Acceptance of MICHI and evaluation of its contents were assessed by means of a process evaluation questionnaire (1=not true to 5=true) and one question that assessed the global evaluation of the program (1=very bad to 10=very good). To assess trends of efficacy, the CDRS-R, the BDI-II, and Item 13 of the CDRS-R were assessed before and after treatment. Furthermore parents filled out a questionnaire about depression scores of their children.

**Results:** The mean attendance rate was 5.33 out of six sessions (88.83%), and adherence to the treatment manual by the trainers was 93%. Participants reported that they liked being in a group and would recommend the program to others, but doubted that the contents learned would be helpful in school or family life. The overall satisfaction rating with the program was 7.21 ($SD=1.89$). Depression scores were significantly reduced pre-to-post treatment (CDRS-R: $F(1,12)=11.76$, $p<.01$; BDI-II: $F(1,32)=11.19$, $p<.01$), as was suicidal ideation ($F(1,33)=4.25$, $p<.05$). However, reduction of depression scores in adolescents was not found in parental ratings.

**Conclusion:** As the results indicated good feasibility and positive response to treatment, we decided to next test the efficacy of MICHI in an RCT.

**3.8. RCT for the assessment of efficacy of MICHI in depressed adolescent outpatients**

RCT for the assessment of efficacy of MICHI in depressed adolescent outpatients

**Introduction:** According to current German guidelines, CBT is one of the first-line interventions for the treatment of depression in minors. Therapy programs for the treatment of depression in adolescents are sparse in Germany, and none has been evaluated in an RCT with a German sample so far. To close this gap, the following study evaluated treatment efficacy of MICHI, a brief group CBT program.

**Methods:** Inclusion and exclusion criteria were the same as in the first and second pilot study (see Sections 3.6 and 3.7). MICHI comprised five regular sessions and one booster session, each lasting 75 minutes ($SD=9.57$) on average. Adherence to the treatment manual by the trainers was 98.24%. Thirty-eight depressed adolescents (30 females), mean age 15.86 years ($SD=1.70$), were randomly assigned to MICHI (PAT-I) or TAU (PAT-W). Instruments for the assessment of efficacy were the CDRS-R and the BDI-II.

**Results:** MICHI participants attended a mean of 5.39 ($SD=.70$) sessions (89.84%). Symptom scores of depression declined in both treatment groups. Interaction effects for time points of measurement (pre/post) and group (PAT-I/PAT-G) were significant with respect to the CDRS-R ($F(1,33)=6.01, p=.02, d_{corrected}=.75$) and the BDI-II ($F(1,33)=4.35, p=.04, d_{corrected}=.39$). Suicidal ideation and behaviour declined in PAT-I. However the interaction effect between group (PAT-I/PAT-W) and time point of measurement (pre/post) was not significant ($F(1,33)=.66, p=.42$). Excluding medicated patients from the analyses did not change the results.

**Discussion:** The results indicated that treatment with MICHI was efficacious compared to TAU. Effect sizes in this study were comparable to effect sizes found for treatment programs that are applied in English-speaking countries. However, in comparison to those programs, MICHI includes only half the number of sessions. Limitations of the present study are the imbalanced sex ratio of the study population, which limits the generalization to the male population. While pharmaceutical treatment had to be stable five weeks prior to start and during the study, it could have biased the results (3 participants were taking Fluoxetine). The PAT-W group received only 1.74 sessions with a child-and adolescent psychiatrist, which is not comparable to the intensity of sessions that the PAT-I group received. However, in our opinion, this reflects TAU in a child- and adolescent psychiatric context.
Neural correlates of successful psychotherapy of depression in adolescents

3.9. Neural correlates of successful psychotherapy of depression in adolescents


**Introduction:** Investigating neural correlates of depression in adolescents may help in adapting therapies to the characteristics and needs of this population. Furthermore, investigating brain activities early in life bypasses the confounding effects of long-term medical treatment or structural changes resulting from a chronic disorder. Both adults and adolescents with depression have been demonstrated to differ from healthy peers with respect to brain activity in the sgACC, amygdala, hippocampus, and frontal cortex. Pre-to-post activity changes in those brain regions were shown to be accompanied with pre-to-post symptom reductions following therapeutic treatment in adults and pharmacological treatment in adolescents and adults. Studies in adolescents are sparse, and changes of neural activity before and after psychotherapy await empirical investigation. As depressed patients tend to overestimate failure and punishment and underestimate success and positive reinforcement, thus demonstrating a dysfunctional reward processing, we used a reward paradigm to assess neural changes according to treatment. In previous studies, this paradigm was shown to reliably activate relevant brain areas.

**Methods:** A total of 22 medication-naïve adolescents diagnosed with a major depressive disorder were assigned to either PAT-W (N=12) or PAT-I (N=10). Eight participants in the PAT-W group participated in MICHI after waiting, resulting in a total of 18 patients who ultimately received MICHI (PAT-I complete; N=18). Pre-to-post activity changes in relevant regions of interest (sgACC, amygdala, hippocampus) were analysed, along with symptom changes assessed by means of the BDI-II and CDRS-R. Interaction effects between group (PAT-I/PAT-W) and time points of measurement (pre/post) were calculated. Furthermore, pre-to-post signal chances and pre-signal activity in the sgACC were correlated with pre-to-post symptom changes.

**Results:** Clinical assessments revealed significant interaction effects with respect to depressive symptoms. In PAT-I but not in PAT-W, significant symptom reductions were accompanied by significant signal changes in the left amygdala, left hippocampus, and right
Neural correlates of successful psychotherapy of depression in adolescents

sgACC, revealing significant interaction effects. Results indicated high correlations between pre-to-post signal reduction in the sgACC, and pre-to-post symptom reduction following BDI-II. Furthermore, bilateral sgACC activity prior to treatment predicted subsequent pre-to-post symptom reduction significantly.

Discussion: Two brain systems are relevant when it comes to depressive disorder: the ventral system, including the amygdala and sgACC, which is important for the identification of emotional stimuli and bottom-up triggering of affective states; and the dorsal system, including the hippocampus, which is important for the top-down regulation of emotional states. A positive correlation between baseline sgACC activity and reduction of depression scores was shown in previous studies, highlighting the importance of the sgACC in the function of a biomarker.
4. General discussion

While prevalence rates of depressive disorders in adolescents were relatively stable between 1965 and 1995 (Costello et al., 2006), the numbers of prescriptions for psychotropic medications and patients being treated in the outpatient setting have increased between 2005 and 2008 (Annuss et al., 2010). Our research determined that the number of F3 (affective disorders) diagnoses of the ICD-10 (classification of mental and behavioral disorders) in adolescent inpatients rose in Germany within 2003 and 2012, as expected, despite a total decline of inpatients. One reason could be increased capacities within the inpatient setting. However, the number of available beds in child and adolescent psychiatric treatment centres declined from 8316 beds in 1991 to 5460 beds in 2010. At the same time, bed occupancy rate increased only slightly from 83.7% in 1991 to 91.7% in 2010 (Boelt & Graf, 2012). A second reason could be that due to a shorter duration of stay, more patients can be treated within a comparable time frame than could be treated previously. This assumption is in line with the finding that minors in 1991 stayed a mean number of 124.7 days and minors in 2010 a mean number of only 39.0 days in the child and adolescent psychiatric treatment centres (Boelt & Graf, 2012). One explanation for shorter stays could be that treatments are more efficacious than in earlier times (Bundespsychotherapeutenkammer, 2014). In contrast to that assumption, Figueroa, Harman and Engberg (2004) postulated that a reduced length of stay might be related to an increased risk of readmission, wherefore increasing numbers wouldn’t reflect a “real” rise in prevalence rates. Elevated readmissions might be especially high in depressed adolescents due to elevated rates of recurrence of depressive disorders (Fombonne et al. 2001). Third, there might be an increased awareness and recognition of symptoms of depression and realization that depression is a prevalent and devastating disorder (Hegerl, 2013) which in turn increases help seeking behaviour (Coppens et al., 2013). If this would be the reason, it would make sense to train community facilitators to improve identification of depressive disorders in minors, as has been previously done in adults (Coppens et al., 2014).

One of the symptoms of depression, which often leads to referral to an inpatient treatment facility, is suicidality, and there is need to identify factors that are associated with this very serious behaviour. In our study (Straub, Keller, Sproeber, Koelch & Plener, 2015) we were able to show that symptoms of mania, above symptoms of depression, were able to predict whether a student reported suicidal ideations and suicide attempts. Concerning
suicide attempts, one more predictor was suicidal ideation. Nock et al. (2009) similarly found a diagnosis of a bipolar disorder to be one of the best predictors for unplanned suicide attempts; however, in the case of suicidal ideation, the authors found the best predictor to be symptoms of depression only. Also differing from our results are those of Resch, Parzer, and Brunner (2008), who found age to be a predictor for both suicidal ideation and suicide attempts. One reason for that finding could be that Resch et al. (2008) included adolescents with a broader age range (11 to 17 years) than we did (14 to 17 years). Our study points to the added value of exploring symptoms of mania in addition to those of depression when assessing suicidal behaviour in adolescents; an aspect that is often neglected in children and adolescents, due to the low prevalence rate (Kozloff et al., 2010) of bipolar symptoms within this age group. The highest prevalence rate for suicide attempts in our study was found in adolescents who reported both elevated symptoms of mania and depression within the previous week. This might support findings in adults that revealed elevated numbers of suicide attempts within mixed episodes (Hawton, Sutton, Haw, Sinclair & Harriss, 2005).

The international gold standard for the structured assessment of depressive symptoms in children and adolescents, as well as for measuring changes in these symptoms, is the CDRS-R (Subica et al., 2014). As criteria for diagnosing depression have not changed essentially from DSM-IV to DSM-5, existing diagnostic instruments can further be applied without any changes. In our study, we found a CDRS-R score of ≥ 36 to indicate a mild to moderate depressive episode following ICD-10 which conforms to our expectations. However, a score of 36 is slightly lower than the score of 40 found by others (Mayes, et al., 2010) which needs to be interpreted in the light of different classification systems: a diagnosis of a major depressive episode based on DSM-IV specifies that the patient has experienced five or more depressive symptoms over a two-week period, whereas a diagnosis based on ICD-10 allows differentiation into mild and moderate if four or six symptoms, respectively, are evidenced. Following the clinical work of Guo et al. (2006), a score of 36 would correspond more to a mild rather than mild to moderate depressive episode. This might be explained by different versions of the CDRS-R (English versus German) as well as by potential cultural differences when it comes to rating psychiatric symptoms such as those of a depressive disorder (Alcantara & Gone, 2014).

The BDI-II is a further frequently used instrument for screening symptoms of depression in adolescents and adults. Nevertheless, it was still unclear as to what extent the
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BDI-II and the CDRS-R scores were correlating and measuring symptoms in a similar way. We identified a correlation coefficient of .67 ($p<.001$) which is high as expected before. However, it is slightly but not significantly, lower than the correlation coefficients found in other studies with healthy or clinically but not exclusively depressed patients (Keller et al., 2012). There are two potential reasons for this. First, our time points of assessment with the two instruments ranged from the same day up to one week apart, whereas other studies assessed them on the same day only. However, the correlation coefficient was .73 in our study when assessments were done on the same day. This coefficient was slightly, but not significantly, higher than .67. Secondly, the BDI-II and CDRS-R were mostly assessed at the start of treatment; and Dorz, Borgherini, Conforti, Scarso and Magni (2004) have shown that the concordance between self-ratings and clinician ratings is poorer in the acute phase of treatment than shortly before discharge. Following Dunlop et al. (2011), the increased concordance over time could be explained through (1) a better shared understanding of symptomatology, (2) a reduction in disorder-specific falsification due to improvement of symptoms, and (3) increasing trust on the part of patient in the therapist, which enables speaking about inner feelings more openly. With respect to correlations on the subscale levels, we did not find a higher correlation for subscales that assessed more objective aspects of depression than for those that assessed more subjective ones as hypothesized. This finding differs from that of Corruble et al. (1999), who found objective subscales to correlate more highly and could possibly be explained by methodological aspects since, unlike us, Corruble et al. (1999) applied a structured interview and a questionnaire with identical questions. Another possible explanation however, is that adolescents speak more openly about their inner feelings than do adults, which needs to be investigated in future studies. With respect to correlations at the item level, we found that items correlated highest when they assessed comparable contents as we expected before, and our correlation coefficients were similar to those found in adult studies (Keller, Ruppe, Stieglitz & Wolfersdorf, 1997). Our finding that the item “suicidal behaviour” correlated the highest and the items “depressive mood” and “concentration problems” the lowest was also reported by Corruble et al. (1999). The high correlation of the item of suicidal behaviour in particular, highlights the opportunity to apply the BDI-II for the screening and assessment of changes in suicidal behaviour. Taken together, the correlation between self-report and structured interview
assessments is high, but there is still some unexplained variance. Therefore one instrument shouldn’t be replaced by the other.

The most recommended form of treatment for children and adolescents with mild to moderate depressive episodes is psychotherapy, either CBT or IPT, while for those with severe depression the recommended treatment is psychotherapy in combination with pharmacological treatment. A review of the literature revealed that despite all the known advantages of a brief group CBT intervention for depressed adolescents, no such program was available in Germany. Furthermore, none of the existing German programs, aimed at depressed adolescents, had been evaluated for efficacy. MICHI was designed to fill this gap.

Since we wished to include subjects with severe depression, which is often accompanied by both an elevated risk for suicidal behaviour and a lowered level of psychosocial functioning, we first evaluated the program in the safer and more structured environment of an inpatient setting. As the results found MICHI to be feasible, well accepted, and to lead to a significant reduction of depressive symptoms and suicidal ideation, we next evaluated it in outpatients, after applying some revisions based on feedback of participants and trainers from the first pilot study. Again, findings were positive. In a final step, MICHI was tested in an RCT with outpatients, with the result of significant interaction effects (group by time points), with small to moderate effect sizes.

In the first pilot study, that was designed to evaluate feasibility and acceptance of MICHI in depressed adolescent inpatients, average attendance was 3.3 sessions out of four regular sessions (82.50%), which is considered as fair. In the second pilot, and the RCT, which both consisted of six sessions conducted in an outpatient setting, a reinforcement system was implemented in an attempt to improve attendance. In the reinforcement system patients received a voucher at the end of the study if they participated in all sessions. In these studies, average attendance of patients in the sessions was 5.33 (88.83%) and 5.39 (89.84%), respectively which was slightly higher than the rate in the inpatient study. However, attendance rates were expected to be higher due to the addition of a reinforcement system. It needs to be taken into account that depressive disorders are often accompanied by a low level of psychosocial functioning which might make it even more difficult for outpatients to make it to sessions. Furthermore, reinforcements might work less in depressed patients than in patients with different mental health problems, due to a reduced sensitivity for reward (Elliott et al., 1997).
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With respect to the group setting, results of the process questionnaire indicated, that participants liked being together with other adolescents and would furthermore recommend the program to others. One reason for this could be that depressed adolescents, in comparison to non-depressed, have fewer contacts with peers and more social deficits, resulting in a higher probability of being socially rejected (Prinstein, Borelli, Cheah & Simon, 2005). A protected group therapy setting with like-minded peers might raise the opportunity for positive social experiences and social contacts. Participants also shared that they felt well understood by and comfortable with the trainers. A positive therapeutic alliance has been shown to be a nonspecific, but very important, factor that could partly explain symptom improvement as well (Martin, Garske & Davis, 2000).

In both pilot studies of MICHI, participants rated the transference of content learned in the program to family life as not being very helpful, expressed doubt that family members would be able to help them with their problems in the future, and did not feel that including them in the program was helpful. One reason could be that during adolescence children increasingly detach from their parents while same-aged peers become more and more important which was also reflected in session 5, in which only one-third of the participants brought a parent while the others brought a friend or sibling instead. A second reason could be that inclusion of family members during only a single session might not be enough to address all skills necessary and maybe the addition of cognitive family therapy sessions might have improved results (Poessel & Hautzinger, 2006).

The therapeutic contents of the MICHI-program were evaluated positively overall in both pilot studies. Specifically, participants of the first pilot study rated “development of an emergency plan” as very helpful, highlighting the need for concrete guidelines on how to behave in case of acute crisis, an element that has been neglected in some other treatment programs. However, they evaluated “relaxation techniques” as being less helpful, which is consistent with the findings of Mattejat et al. (2010) who stated that relaxation techniques are of little help in patients with depression, as patients start to ruminate and focusing on their sad feelings during relaxation. Based on this feedback, relaxation techniques were eliminated from the program.

Concerning fidelity of implementation with respect to the trainers, there was an increase in adherence to the treatment manual from the second pilot (93%) to the randomized controlled study (98.24%). This may have been due to continuous supervision,
to the detailed instructions provided in the treatment manual, and to increasing familiarity by the trainers with the program’s contents. Treatment adherence was comparable to the one of other manualized treatment programs ranging from 80% to 94% (Gaynor & Lawrence, 2002; Kahn, Kehle, Jenson & Clark, 1990; Listug-Lunde, Vogeltanz-Holm & Collins, 2013; Rossello, Bernal & Rivera-Medina, 2008).

Pre-post-test comparisons of the first pilot study as well as both pre-post and follow-up analyses of the second pilot study indicated significant improvements of depressive symptoms, with effect sizes ranging from small (for self-ratings) to moderate (for structured interview assessments). The remission rate in the intervention group (with remission defined as a CDRS-R score <36) was 42% in the second pilot study and 47.37% in the RCT, which is comparable to the rates of 45.2% and 56.0% reported by others (Ihle, Jahn, Spieß & Herrle, 2002; Ihle & Jahnke, 2003), who had evaluated the German version of the group treatment program CWD-A in a pre-post-test design. These rates are also comparable to those of 39–62% that have been reported in international studies that aimed to evaluate CBT therapies for the treatment of depressed adolescents (Kahn et al., 1990; Rohde, Clarke, Mace, Jorgensen & Seeley, 2004; Rossello et al., 2008). However, this comparison needs to be interpreted with caution, as the definition of reliable remission differs between studies.

With respect to the RCT study, pre-to-post depressive symptoms decreased in both the intervention and the waiting control group, however the decrease was greater in the intervention group. One possible explanation is that the control group also received treatment, and another is the high rate of spontaneous remission that is often seen in depressive disorders in childhood and adolescence (Whiteford et al., 2013). The interaction effects (group by time points of measurement) were significant with respect to both the CDRS-R with moderate effect sizes ($d_{\text{corrected}}=.75$) and the BDI-II, with small effect sizes ($d_{\text{corrected}}=.39$). As MICHI is the first program for the treatment of depression in adolescents that has been evaluated by means of an RCT in a German sample; its efficacy can only be compared to international programs at this time. The therapy program of Harrington (2001), which is conceptualized for individual treatment, was found by Wood et al. (1996) with an effect size of .73, while effect sizes of the group treatment program CWD-A were found to range between .02 (Clarke et al., 2002) and 1.34 (Kahn et al., 1990), depending on the control group. This needs to be interpreted in conjunction with the fact that MICHI is two to four times shorter than other treatment programs (Abel & Hautzinger, 2013; Ihle & Herrle, 2011).
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Furthermore, our results are in line with the result of the meta-analysis of Cuijpers et al. (2013), which reported a weak relationship between efficacy and duration of treatment but a strong one between efficacy and weekly intensity of therapy. This finding also supports the dose effects model which states that 41% of the patients improve after four psychotherapeutic sessions and 53% after eight (Howard et al., 1986). Supporting this model, Stulz, Lutz, Leach, Luco and Barkham (2007), working with two groups of highly impaired clients, found that one group improved strongly ($d=2.23$) within the first sessions of psychotherapy (<14 sessions). The other group however, improved slowly within the first sessions (<14; $d=.30$) and also slowly during the remainder of the treatment, despite long treatment durations (98% had >14 sessions). Taken together it appears as if there are two categories, fast and slow responders. Based on those findings, one recommendation could be that all patients start with a brief but intense psychotherapeutic treatment; and for those who do not respond, a change in treatment (e.g. initiation of pharmacological treatment) should be considered as recommended by the NICE guidelines (National Collaborating Centre for Mental Health, 2005).

In consideration to parental reports in the pilot studies of MICHI, there was no significant pre-post-test effect. These results are comparable to those of Weisz et al. (2006), who doubted that parents are good informants with respect to affective symptoms of their children.

In both MICHI pilot studies and the RCT, suicidal ideation declined significantly from pre to post. Concerning participants of all three studies, 53.10% revealed moderate to severe suicidal ideation before and only 21.72% after treatment on average. Given that in a study of healthy European adolescents aged 14 to 16 years (Resch et al., 2010), 17% of females and 8.3% of males reported having had suicidal ideation within the last two weeks, the percentage of adolescents with post-intervention suicidal ideation in our sample was comparable to that seen in non-clinical populations. We also found a significant decline of pre-to-post suicidal ideation in the RCT, with a non-significant interaction effect between group and time points of measurement. Others (Brunstein-Klomek & Stanley, 2007; Kapusta, Fegert, Haring & Plener, 2013) have found comparable effects: a reduction of suicidal ideation after psychosocial treatment that was strong but not significantly different from the active control group.
Besides feasibility and efficacy of MICHI, we also studied neural correlates of effective psychotherapeutic treatment of adolescent depression. Reduction in clinical symptoms was found to be accompanied by significant changes in brain activation in the left amygdala, left hippocampus, and right sgACC revealing significant interaction effects between group (PAT-I/PAT-W) and time points of measurement (pre/post). Furthermore pre-to-post signal changes in the sgACC correlated highly with pre-to-post symptom changes in the BDI-II and pre-treatment sgACC activity was able to predict subsequent treatment response. Change of activity in the amygdala pre-to-post treatment is in line with one of the few studies on neural effects of psychotherapy in adults. Fu et al. (2008) for example showed that activity of the amygdala changed in parallel with symptom improvement following a short, but clinically successful, psychotherapy. The amygdala was thereby confirmed as an important brain structure for the identification of emotional states as well as for bottom-up modulation of affective states (A. G. Phillips, Ahn & Howland, 2003).

Our findings were furthermore consistent with those reported in depressed adults after a pharmacological intervention, which included a significant reduction in hippocampus activity after treatment with paroxetine over six weeks (Kennedy et al., 2001), with fluoxetine over eight weeks (Fu et al., 2007), and after CBT (Fu et al., 2008), with significant interaction effects seen between group and time points of measurement. A conflicting finding was that of Goldapple et al. (2004) who found a relative increase in metabolic activity in the hippocampus following CBT where our results pointed towards a decrease; however, different findings can possibly be explained by the application of different paradigms. As the hippocampus is a region that contributes to emotional memory (Tahmasian et al., 2013), in which cognitive processes are integrated, and which can be biased by emotional input, it has been suggested that it contributes to executive functions, including effortful regulation of affective states (M. L. Phillips et al., 2003), which in turn may be particularly sensitive to cognitive interventions. Changes in hippocampal activation following psychotherapy may reflect the ability of psychotherapy to modulate activation in key nodes of networks mediating top-down processes.

The ACC plays a critical role in the expression and modulation of emotion (Papez, 1995) and in the regulation of limbic activity (Mayberg, 2003). The sgACC has been shown to be important for the identification as well as bottom-up modulation of affective states (M. L. Phillips et al., 2003). Activation of the sgACC has consistently been related to the clinical
response to different antidepressant treatments, including SSRIs in both adults (Mayberg et al., 2000) and adolescents (R. Tao et al., 2012), to electroconvulsive therapy, to repetitive transcranial magnetic stimulation, and to ablative surgery (Mayberg et al., 2005), which highlights its role as a key structure in depression. Also, with respect to psychotherapeutic treatment effects, Yoshimura et al. (2013) found activity in the vACC to be increased for positive stimuli and decreased for negative stimuli after CBT in depressed adult patients.

In our study, relatively increased pre-treatment activity in the sgACC was associated with subsequent treatment response, a finding that has also been shown for pharmacological treatment response in other studies (Fu et al., 2004; Goldapple et al., 2004; Kennedy et al., 2001; Mayberg et al., 2000). In support of our results, Yoshimura et al. (2013) found a negative correlation between signal change in the vACC and improvement of depressive symptoms. In contrast, Konarski et al. (2009) found that non-responders, in comparison to responders, exhibited pre-treatment hypermetabolism in the sgACC; and Siegle et al. (2006) reported a significant association between reduced pre-treatment sgACC activity and subsequent treatment response. Different findings could be explained by the different paradigms applied; for example, Siegle et al. had focused on negative stimuli (-activity), while we focused on the contrast between positive and negative stimuli ((+ activity) – (- activity) = (+ activity)).

The named brain areas above were shown to be modulated by pharmacological treatment in depressed patients (Arnone et al., 2012, Godlewska et al., 2012, Sheline et al., 2001) however revealed similar effects in healthy subjects after placebo as well (Abler et al., 2011; Macoveanu, 2014). Therefore there is some ambiguity about its underlying factors (symptom, improvement and/or medication). In agreement with one of the rare studies on neural effects of psychotherapeutic treatment in adults (Fu et al., 2008), we were able to show that activity in the amygdala, sgACC and hippocampus changed in line with symptom improvement after a clinically efficacious psychotherapy, but not in the depressed waitlist control group. As our subjects were naïve to pharmacological treatment, present results support the notion that neural activity changes are most likely related to treatment success in general rather than to specific pharmacological treatment effects.

Studies that have mainly investigated both pharmacological (Fu et al., 2008; Goldapple et al., 2004; R. Tao et al., 2012) and psychotherapeutic treatment effects (Brody et al., 2001; Goldapple et al., 2004; Ritchey et al., 2011) in adults, have found altered pre-
to-post treatment activity changes in the prefrontal cortex, but we were not able to replicate those findings. One explanation could be that all studies listed above used either an emotional picture/emotional word or a resting state paradigm. It might be assumed that these paradigms are better suited to map activation changes in the prefrontal cortex, as this brain region is associated with self-referential or other-referential processing of emotional stimuli (Yoshimura et al., 2009), as, for example, a reward paradigm. However, one study that used a reward paradigm in adults to assess signal changes before and after an average of 11 sessions of BAT (Dichter et al., 2009) also revealed functional changes in the orbitofrontal gyrus.

A second explanation could be that, as most of the above-mentioned studies were done in adults, it could be hypothesized that signal changes in the prefrontal cortex might be more difficult to detect in adolescents due to heterogeneous states of maturation (Casey et al., 2008). Contrarily, Tao et al. (2012) found treatment effects with fluoxetine within the orbitofrontal cortex in adolescents as well who were of a comparable age range (11–18 years) to those in our study (13–18 years).

Thirdly, a reason for diverse findings could lay in different reward paradigms applied. Dichter et al. (2009) for example used the “Wheel of Fortune” reward paradigm which might be better suited for the illustration of psychotherapeutic treatment effects, with respect to prefrontal cortex areas, than the reward paradigm that we applied. However, Abler, Erk & Walter (2007), who also applied a monetary incentive delayed task, found activity reduced in the inferior frontal cortex after dopaminergic medication but not placebo, indicating that this task is well suited to display treatment effects as well.

Fourth, activity changes in the studies of both Tao et al. (2012) and Dichter et al. (2009) occurred after eight weeks of fluoxetine and 11 weeks of BAT, respectively. It could be assumed that due to the brevity (only five weeks) of the psychotherapeutic treatment MICH, effects might be detectable sooner within subcortical brain areas than within cortical ones, as changes might occur more quickly in regions that are relevant for bottom-up than for top-down processing.

4.1 Limitations
In the study that looked at increasing numbers of F diagnoses in the inpatient setting from 2003 to 2012, the main diagnoses might rather be based on the judgement of the clinician
than on standardized instruments (e.g., structured interviews). Furthermore different classification systems (DSM or ICD) might have been used, influencing results as well. Therefore, the quality of routine data from health systems may have some weakness concerning validity of diagnoses (Dolle, Schulte-Koerne, von Hofacker, Izat & Allgaier, 2012).

With respect to the study that assessed the relationship between depression/mania symptoms and lifetime suicidality, we cannot draw conclusions about the relationship between bipolar disorder and suicidality directly. This is because we assessed symptoms of mania and depression over the previous week by means of questionnaires in a cross-sectional design, which neither measured the required time frame following ICD-10 (e.g., two weeks for depressive disorders), nor allowed us to obtain information about the course of the episode (e.g., whether episodes of depression and mania were altered). Furthermore, questionnaires instead of structured interviews were used, which might hamper validity of diagnoses.

Concerning the study that looked at convergence between CDRS-R and clinical diagnosis, results are limited due to the small sample size of raters as well as the great diversity of professions within each group. Furthermore not all of them were trained in the execution of the CDRS-R beforehand. It would also have been beneficial to conduct the same procedure with more than one videotaped structured interview displaying different types of severity of depressive disorder.

In the study that compared symptoms of depression on the sum score, subscale and item level, assessed by means of the CDRS-R and BDI-II, both instruments were conceptualized for the assessment of depression but they are not identical with respect to item content and wording. Furthermore, instruments were not assessed on the same day, but within one week and mostly directly after referral to the child and adolescent psychiatry. Those aspects could have potentially affected correlational strength. With respect to third variables, we only focused on age, sex, IQ, and treatment setting.

Both pilot studies primarily aimed to reveal information about acceptance and feasibility of MICHI. However, findings concerning pre-to-post symptom improvement in both pilot studies of MICHI must be interpreted with caution. The small number of participants and the absence of a waiting control group, and of a randomized group assignment, hampers conclusions about treatment efficacy. In the first pilot study, a further limitation is the inability to separate effects of MICHI from the inpatient treatment setting.
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Another limitation, that affects both pilot studies and the RCT, is the inclusion of participants taking antidepressant medications. We attempted to reduce this impact by including only individuals whose regimen had been stable for three to five weeks prior to the start and during the study. The inclusion of patients who are not medication-naïve was chosen as it presents a naturalistic setting which is closer to a clinical real-life situation. Furthermore, the instruments that were applied for the assessment of the contents of MICHI were conceptualized by our own team under supervision however, they were not checked for psychometric properties beforehand.

With regard to the RCT and fMRI study, the treatment received during the waiting period by the control group comprised about two half-hour appointments with a psychologist or psychiatrist. This cannot be put on the same level as an active control group, as TAU was comparatively less intense than MICHI and was not applied in a standardized manner. However, in our opinion this procedure reflects TAU reality in a German child and adolescent psychiatry.

With respect to the fMRI study, we compared pre-to-post effects of PAT-I ($N=10$) with pre-to-post effects of PAT-W ($N=12$). Due to small sample sizes, we were forced to include all participants who received the intervention after waiting for within-group analyses. Therefore, of the 18 subjects included in the pre-post-follow-up-test analyses, eight had been assigned to the waiting control group prior to receiving the intervention. Potentially the symptoms of these 8 participants may have improved during the waiting period through spontaneous recovery (Whiteford, et al., 2013), which is not ideal with respect to scientific standards. However, those participants of the waiting group who were later admitted to participate in psychotherapy did not differ in CDRS-R raw sum scores from participants randomly assigned to the immediate intervention group (PAT-I).

Two further aspects that affected all four previous studies, aimed to evaluate MICHI and its neural correlates, were 1) a skewed gender recruitment (females=75%, males=25%), which limits generalizability to males; and 2) inclusion of participants with co-morbid disorders. On the one hand, both of these aspects could affect efficacy, but on the other, they reflect treatment reality. A final factor is that patients were permitted to speak to the trainer individually after a therapeutic or diagnostic session in case of an acute crisis. This opportunity was used only a few times, but could still have influenced outcomes. This issue was discussed beforehand and was found to be a necessary supplement for ethical reasons.
4.2 Conclusions and perspectives
Rates of depressive disorders in minors remained stable between 1965 and 1996 however numbers of emotional problems in 11 to 17 year olds rose between 2003-2006 and 2009-2012. Furthermore, the number of pharmacological and outpatient treatments increased. In line with those findings, we showed that inpatient treatment for F3 diagnoses rose as well even after controlling for decrease of the total numbers of patients. Future studies, assessing the course of the number of patients being treated in the inpatient setting, should ensure that diagnoses are assessed by standardized diagnostic instruments (e.g. structured interviews). Furthermore, studies should identify reasons for the increasing numbers of inpatients (e.g. increased awareness for depressive symptoms in minors in both, the population and primary health care). Furthermore, more recent meta-analyses are needed about the course of prevalence rates of depressive disorders in Germany referring to the last ten years. However there are two barriers in doing so: first of all, clinicians apply different coding practices and use different classification systems (DSM, ICD). Second, alterations of existing classification systems (e.g. from DSM-IV to DSM-5) also affect prevalence rates. (e.g., some children, that would have been diagnosed with depressive disorder according to DSM-IV might now be diagnosed with disruptive mood dysregulation disorder following DSM-5 (Plener, Witt, Straub & Fegert, 2013)).

Considering symptoms of mania in addition to those of depression and their association with suicidality, we were able to show that suicidal ideation was best predicted by symptoms of depression, and above that by symptoms of mania, while suicide attempts were best predicted by symptoms of depression and above that by symptoms of mania and age. This points to the added value of specifically exploring symptoms of mania in addition to those of depression (both symptoms of the ICD-10 chapter F3 “affective disorders”) when assessing suicidal behaviour in adolescents. Prospectively, it would be interesting to assess the relationship between bipolar disorders (diagnoses should be done by means of structured interviews) and suicidal behaviour in a longitudinal design. Additionally, it should be analysed also in minors whether suicide attempts rather occur during depressive or mixed episodes than during episodes of mania, as was shown in adults (Hawton et al., 2005).

Our study, the first to assess the concordance between the clinical diagnoses of a depressive episode following ICD-10 and CDRS-R scores of the German version, found a CDRS-R value of greater than 36 to be indicative of a mild depressive episode. As most of the
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literature on the CDRS-R refers to samples in the United States, which compared interview raw scores to diagnostic criteria of major depression following DSM-IV, there is a need for further studies on convergence of CDRS-R scores and diagnoses according to ICD-10, especially with its classification into moderate and severe depressive episodes. In doing so, future studies should involve larger sample sizes of clinical experts rating interviews with a wider range of videotaped structured interviews displaying various severities of depressive disorders.

Sum scores of the BDI-II and CDRS-R correlated highly but not completely, indicating that they measure similar, but not identical aspects of depression. On the item level, items with related content, such as those dealing with suicidal ideation, were found to correlate higher than did less related ones. On the subscale level, subscales measuring more objective aspects of depression did not correlate higher than subscales measuring more subjective aspects not supporting the finding of Corruble et al. (1999). Further studies should assess whether this finding can be attributed to the assumption that adolescents tend to speak more openly about their inner feelings than do adults where subscales measuring objective and subjective contents were comparable. Dunlop et al. (2011) reported that in adults the discrepancy between self-report and clinical assessment is higher at the beginning of treatment than at the end. Therefore, it would be interesting to calculate concordance of self-report questionnaires and structured interviews at both the beginning and end of treatment, and to compare both values to see whether this assumption is also true for adolescents. Further studies should identify factors that affect correlational strength such as level of knowledge about symptoms of depression or shame with respect to answering questions about depression openly in a structured interview.

The longer the duration of a depressive episode, the higher the chances for relapses in adulthood. This highlights the need for brief and effective treatments of depression at its beginnings. Prior to the development of MICHI, the only programs available in Germany for the treatment of depressed adolescents lasted an average of 12 sessions and were conceptualized for the treatment of mild to moderate depression; furthermore, none had been evaluated in a randomized controlled design. To close this gap we developed a brief cognitive behavioural group psychotherapy called MICHI. It was assessed in a step-wise manner (inpatient pilot study, then outpatient pilot study, then outpatient RCT) and shown to be feasible, accepted, and efficacious. The small to moderate effect sizes found for MICHI
are comparable to those found for English-language CBT programs which last two to four times longer than MICHI supporting the dose-effect model of negative acceleration (Howard, et al., 1986). However, future studies should aim to identify characteristics of patients who might profit from shorter lasting treatments and characteristics of patients who might profit from longer lasting treatments. Besides that, forthcoming studies should investigate MICHI in a multicentre study, comparing the treatment arm with a more active waiting control group and adding follow-up measurements up to six to 12 months after termination of psychotherapy, to investigate long-term effects. The further addition of cognitive behavioural family therapy components (Poessel & Hautzinger, 2006) might possibly be helpful, and needs to be explored in future studies. As the goal of integrating family or friends into the program was to prevent relapse, which would more likely be necessary sometime in the future rather than right after completion of the program, this aspect should be evaluated in the long-term rather than the short-term. Furthermore, psychosocial functioning level could be chosen as one more outcome parameter besides depression scores.

As prevalence rates of depression are rising from childhood to adolescence, there is a strong need to improve our knowledge about the underlying processes of depression during this vulnerable period. Studying the neurobiology of depression in adolescents allows us to avoid confounds that exist in studies with adults with respect to long-term medication, neural changes due to relapses, or chronic course of the disorder. Worldwide, this is the first study that has investigated neural correlates of successful psychotherapeutic treatment of depression in adolescents as compared to a waiting group. Activation of the amygdala, hippocampus, and sgACC, three areas that are commonly reported as relevant in depression, were found to change with amelioration of depressive symptoms compared to those who received only minimal wait-list treatment. Pre-treatment activity in the sgACC was related to subsequent treatment response. The amygdala, sgACC and hippocampus were shown to be relevant with respect to processing of negative stimuli, of ruminative thoughts and of biased memory for negative stimuli in individuals with depression (Disner, Breevers, Haigh & Beck, 2011) – aspects that seem to have been successfully tackled by CBT. More globally, the amygdala and sgACC are important brain structures for the identification and bottom-up modulation of affective states, while the hippocampus is more important for top-down regulation. Therefore, our study supports models suggesting that dysfunctional neural
mechanisms of emotion regulation in depression can be targeted by psychotherapy, at least in the early stages of the illness, and may therefore constitute a state rather than a trait marker. In future studies, neural correlates should be investigated with a larger sample size, and it would be interesting to see whether effects remain stable in the long-term. In addition, brief interventions should be compared with longer lasting therapies to reveal information about how many sessions are needed to find neural correlates of successful treatment in the prefrontal cortex as well. Furthermore, it would be interesting to compare neural correlates of pharmacological versus psychotherapeutic treatment in adolescents as well. As functional connectivity was shown to give valuable information about whether a subject was clinically depressed or not (Craddock, Holtzheimer, Hu & Mayberg, 2009), future studies should investigate functional connectivity and its changes as potential biomarkers and putative treatment effects.

A proper diagnosis of depression requires a valid and reliable assessment, which is provided by the German version of the CDRS-R. Furthermore, it is necessary to understand underlying factors of suicidality to improve prevention of suicidal events – often reasons for referral to the inpatient setting. Elevated rates of minors, being treated because of mood disorders in the out- and inpatient setting, highlight the need for fast, available, and efficacious treatments. MICHI is the first therapy program whose efficacy has been shown on both the psychometric and neural levels. Our finding of a strong correlation between individual expressions of brain activation and subsequent treatment response may be one more step towards being able to identify certain bio-types to aid in the decision as to which form of treatment is the most suitable for a given individual. The finding that a brief but intense program can be helpful when it comes to treating depression in adolescents carries several advantages. First, brief interventions in comparison to longer-lasting ones can reduce barriers of psychotherapeutic health care utilization, as they can be more easily integrated into daily lives. Second, the fact that the effects of a brief intervention are comparable to a longer-lasting psychotherapy has both economic and political advantages. Based on the present findings, and taking into account long waiting periods for psychotherapeutic treatments in Germany on the one hand and strong need for treatments on the other, a brief intervention could serve as a first-line treatment, reserving longer-lasting psychotherapies or pharmacological treatment for those who fail to respond.
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References


References


References

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6 Original research articles

6.1 Treatment of mental diseases in children in German hospitals: analysis of frequencies in the years 2003 to 2012.

Main authors’ contributions to the article:
P.L. Plener and F. Keller managed data acquisition, executed statistical analyses, and interpreted statistical outcomes. P.L. Plener wrote the manuscript, integrated remarks of the co-authors, and revised the manuscript according to reviewer’s comments.

Contribution of J. Straub to the article:
J. Straub researched literature and wrote parts of the manuscript. She and her co-author helped with revising the manuscript according to the reviewer’s comments.

Reference

Behandlung psychischer Erkrankungen von Kindern in deutschen Krankenhäusern

Analyse der Häufigkeiten der Jahre 2003 bis 2012

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Schlüsselwörter
Stationäre Behandlungen, Kinder- und Jugendpsychiatrie, Diagnosen, psychiatrische Erkrankungen, Deutschland

Zusammenfassung

Keywords
Inpatient treatment, child and adolescent psychiatry, diagnoses, psychiatric disorders, Germany

Summary
Recent data from the nationwide German KiGGS survey show a stable level of psychiatric and behavioural symptoms in a community sample. Nevertheless, rates of psychopharmacological treatment in childhood and adolescence are increasing. This study analyses the prevalence of ICD-10 chapter F diagnoses, from German hospitals in children up to the age of 15 in the years 2003 to 2012. There was a significant increase in most diagnostic groups with the exception of organic (F0), schizophrenic (F2), personality and behavioral disorders (F6) and mental retardation (F7), showing stable or even decreasing rates of hospital treatments in a 10 year time frame.

- 3 bis 6 Jahre wiesen in der Basisehebung 19,3% der Teilnehmer ein erhöhtes Risiko für psychische Auffälligkeiten und in der ersten Welle nur 17,2% (p = 0,158) auf;
- 7 bis 10 Jahre waren dies in der Basisehebung 22,6%, in der ersten Welle 23,1% (p = 0,750);
- 11 bis 13 Jahre waren dies in der Basisehebung 21,5%, in der ersten Welle 23,3% (p = 0,256).

Getrennt nach Altersgruppen zeigten sich in der differenzierten Analyse der SDQ-Subskalen eine Zunahme von Verhaltensproblemen von einem Mittelwert von 2,1 auf 2,4 (p < 0,001) und eine Abnahme des Bereichs Peer-Probleme von 1,4 auf 1,2 (p < 0,001) in der Altersgruppe der 3- bis 6-Jährigen. Ebenso fand sich eine Zunahme des Bereichs Verhaltensprobleme in der Altersgruppe 7 bis 10 Jahre (von 2,0 auf 2,2; p = 0,001). Eine Zunahme der emotionalen Probleme zeigte sich in der Altersgruppe der 11- bis 13-Jährigen (von 2,0 auf 2,2; p = 0,001). In allen Altersgruppen von 3 bis 13 Jahren fand sich eine Zunahme des proszialen Verhaltens (p < 0,001 in allen Altersgruppen).

In einer Metaanalyse von 33 Studien zu emotionalen und Verhaltensstörungen bei...
deutschen Kindern und Jugendlichen aus über 50 Jahren unter Beteiligung von 72978 Kindern und Jugendlichen aus nicht klinischen Stichproben wurde eine zusammengesetzte Prävalenz von 17,6% für emotionale und Verhaltensstörungen berichtet.

Im Vergleich der Häufigkeiten über die Zeit, die jedoch aufgrund des unterschiedlichen methodischen Vorgehens nur eingeschränkt vergleichbar waren, zeigte sich kein Anstieg der Auffälligkeiten in den Studien über die Jahre (3).

Ahnlich wie in der KiGGS-Studie, konnten auch Lehmkuhl et al. (12) in einer zufällig ausgewählten Versichertenstichprobe von 55545 Kindern und Jugendlichen im Jahre 2006 bei 19,3% der Kinder und Jugendlichen zwischen 0 und 18 Jahren einen psychiatrischen Behandlungsanlass feststellen, wobei bei ungefähr einem Drittel mehr als eine psychiatrische Diagnose vorlag. Dem gegenübergestellt zeigte eine Umfrage bei Eltern schulpflichtiger Kinder, dass lediglich etwa 10% der Kinder psychotherapeutische Behandlung erhielten (13).

Auch die KiGGS-Studie belegt, dass nur etwa die Hälfte der als psychisch krank diagnostizierten Kinder zurzeit behandelt werden (15). Neben anderen Gründen (z. B. Angst vor Stigmatisierung) ist dies auf den tatsächlichen Mangel an Behandlungskapazitäten zurückzuführen.


Neben der Zunahme ambulanter Psychotherapie wurde in Deutschland auch ein Anstieg der psychopharmakologischen Behandlung von Kindern und Jugendlichen, etwa mit atypischen Antipsychotika, beschrieben. In einer Analyse einer großen deutschen gesetzlichen Versicherung zeigte sich etwa ein Zuwachs der Antipsychotika-Verschreibungen in der Altersgruppe der 10- bis 14-Jährigen von 0,24% auf 0,43% zwischen 2005 und 2012 (2).


**Methode**

Die Angaben erstrecken sich auf alle Krankenhäuser nach § 1 Abs. 3 Nr. 1 KHSstaV im gesamten Bundesgebiet, die jährlich zu ihren erzeugten Diagnosedaten schriftlich und mit Auskunftspflicht befragt werden. Die Daten werden an das Landesamt für Statistik übermittelt, dort elektronisch erfasst und hinsichtlich Plausibilität geprüft. Anschließend erfolgt die Übermittlung der aggregierten Landesergebnisse an das statistische Bundesamt (www.destatis.de).


**Ergebnisse**

Von 2003 bis 2012 kam es zum Anstieg der F-Diagnosen bei den 0- bis 15-Jährigen (Tab. 1, Abb. 1), wobei dieser in beiden Geschlechtern präsent war. Er war insgesamt (Steigung 1050/Jahr, p < 0,001) und sowohl bei männlichen (Steigung 592/Jahr, p < 0,001) als auch weiblichen (Steigung 458/Jahr, p < 0,001) Kindern ausgesprochen. Auch nach Korrektur der abfallenden Gesamtzahl an 0- bis 15-Jährigen in Deutschland (12112000 in 2003 gegenüber 10492000 in 2012) blieb weiterhin die steigende Zahl der F-Diagnosen signifikant (p = 0,002).

In der Betrachtung der einzelnen Untergruppen der Kapitel F der ICD-10 bei den 0- bis 15-Jährigen ergibt sich ein differenziertes Bild (Abb. 1b), wobei es einige Kategorien gibt, deren Häufigkeit im 10-Jahreszeitraum konstant bleibt, während in anderen Kategorien ein deutlicher Anstieg zu verzeichnen ist (Tab. 2).

- Ein Anstieg ist in den Kategorien F1, F3, F4, F5, F8 und F9 zu verzeichnen, am
### Tab. 1 Altersverteilung der F-Diagnosen im Krankenhaus nach Jahren

<table>
<thead>
<tr>
<th>Jahr</th>
<th>männlich</th>
<th></th>
<th></th>
<th></th>
<th>weiblich</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt; 1 Jahr</td>
<td>1–5 Jahre</td>
<td>5–10 Jahre</td>
<td>10–15 Jahre</td>
<td>&lt; 1 Jahr</td>
<td>1–5 Jahre</td>
<td>5–10 Jahre</td>
<td>10–15 Jahre</td>
<td>gesamt</td>
</tr>
<tr>
<td>2003</td>
<td>835</td>
<td>3141</td>
<td>7349</td>
<td>12965</td>
<td>820</td>
<td>2035</td>
<td>3354</td>
<td>11056</td>
<td>41555</td>
</tr>
<tr>
<td>2004</td>
<td>762</td>
<td>3280</td>
<td>7891</td>
<td>13057</td>
<td>696</td>
<td>2054</td>
<td>3470</td>
<td>11720</td>
<td>43007</td>
</tr>
<tr>
<td>2005</td>
<td>644</td>
<td>2974</td>
<td>7957</td>
<td>13058</td>
<td>648</td>
<td>1825</td>
<td>3404</td>
<td>11582</td>
<td>42282</td>
</tr>
<tr>
<td>2006</td>
<td>560</td>
<td>2862</td>
<td>8270</td>
<td>12879</td>
<td>483</td>
<td>1800</td>
<td>3641</td>
<td>11823</td>
<td>42318</td>
</tr>
<tr>
<td>2007</td>
<td>485</td>
<td>2793</td>
<td>8654</td>
<td>13685</td>
<td>419</td>
<td>1631</td>
<td>3689</td>
<td>12743</td>
<td>44099</td>
</tr>
<tr>
<td>2008</td>
<td>554</td>
<td>3084</td>
<td>8915</td>
<td>14544</td>
<td>515</td>
<td>1824</td>
<td>3886</td>
<td>13507</td>
<td>46829</td>
</tr>
<tr>
<td>2009</td>
<td>526</td>
<td>2926</td>
<td>9131</td>
<td>14859</td>
<td>510</td>
<td>1725</td>
<td>3812</td>
<td>13504</td>
<td>46993</td>
</tr>
<tr>
<td>2010</td>
<td>494</td>
<td>2907</td>
<td>8999</td>
<td>15211</td>
<td>443</td>
<td>1707</td>
<td>3833</td>
<td>14931</td>
<td>48525</td>
</tr>
<tr>
<td>2011</td>
<td>524</td>
<td>2994</td>
<td>8781</td>
<td>15488</td>
<td>463</td>
<td>1682</td>
<td>3906</td>
<td>15830</td>
<td>49668</td>
</tr>
<tr>
<td>2012</td>
<td>484</td>
<td>2952</td>
<td>8769</td>
<td>15593</td>
<td>455</td>
<td>1738</td>
<td>3589</td>
<td>16723</td>
<td>50303</td>
</tr>
</tbody>
</table>

### Abb. 1 Krankenhausdiagnosen der Jahre 2003 bis 2012 in der Altersgruppe 0 bis 15

- a) Kategorie F (gesamt und nach Geschlecht)
- b) Kategorien F0 bis F8
- c) Kategorien F90.x bis F99.x
- d) Kategorie F in alten und neuen Bundesländern
- Eine Abnahme der Diagnosehäufigkeit findet sich in den Kategorien F0, F6 und F7. Die Abnahme in den Kategorien F6 und F7 erreicht statistische Signifikanz (Tab. 2).

Betrachtet man aufgrund des Lebensalters (0 bis 15 Jahre), die Kategorie F9 differenziert und um zu ergründen, welche Subkategorien den starken Anstieg verursachen, so zeigt sich in vielen, nicht in allen – Kategorien ein deutlicher Anstieg in den Jahren 2003 bis 2012 (Abb. 1c). In der Betrachtung der F9-Subkategorien zeigt sich eine Steigerung in den Kategorien F90, F92, F93, F94 und F95, während die Häufigkeiten in den Kategorien F91, F98 und F99 gleich bleiben (Tab. 2). Um geografische Unterschiede bewerten zu können, erfolgte eine Analyse nach Bundesländern. Dabei zeigte sich mit Ausnahme von Bremen, dem Saarland, Sachsen-Anhalt und Schleswig-Holstein eine signifikante Zunahme (Tab. 3).

**Diskussion**

In unserer Arbeit analysierten wir die Krankenhausbehandlungen aufgrund einer F-Diagnose bei Kindern im Alter von 0 bis 15 Jahren in Deutschland im Zeitraum 2003 bis 2012. Dies ergab eine signifikante Zunahme der Häufigkeiten von F-Diagnosen gemäß ICD-10. Diese Zunahme war in beiden Geschlechtergruppen und vor allem in den Kategorien F1, F3, F4, F5, F8 und F9 ausgesprochen. Während der Zahlen psychischer Erkrankungen aus dem schizophrenen Formenkreis (F2) und bei organischen Ursachen (F0) ein stabiles Niveau erreichten, und bei Persönlichkeitsstörungen (F6) und Intelligenzminderung eine abnehmende Diagnosehäufigkeit zu finden waren.

Hinsichtlich der F-Diagnosen könnte spekuliert werden, dass die Prävalenz von Erkrankungen mit hoher Heritabilität (z. B. bei F2-Diagnosen) nur geringen Schwankungen unterworfen sind. Dagegen spricht jedoch die Zunahme von Erkrankungen, die ebenso eine hohe Heritabilität aufweisen.

### Tab. 2 Steigerung der F-Kategorie und F9-Subkategorien der Krankenhausdiagnosen bei 0- bis 15-Jährigen in den Jahren 2003 bis 2012

<table>
<thead>
<tr>
<th>Kategorie</th>
<th>Steigungscoefficient</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>F0</td>
<td>Organische einschl. symptomatiche psychiatrische Störungen</td>
<td>−7,43</td>
</tr>
<tr>
<td>F1</td>
<td>Psych. u. Verhaltensstörungen durch psychotrope Substanzen</td>
<td>148,50</td>
</tr>
<tr>
<td>F2</td>
<td>Schizophrenie, schizotype und wahnhafte Störungen</td>
<td>2,07</td>
</tr>
<tr>
<td>F3</td>
<td>Affektive Störungen</td>
<td>179,28</td>
</tr>
<tr>
<td>F4</td>
<td>Neurotische, Belastungs- und somatoforme Störungen</td>
<td>186,88</td>
</tr>
<tr>
<td>F5</td>
<td>Verhaltensauffälligkeiten mit körperlichen Störungen und Faktoren</td>
<td>39,99</td>
</tr>
<tr>
<td>F6</td>
<td>Persönlichkeits- und Verhaltensstörungen</td>
<td>−18,42</td>
</tr>
<tr>
<td>F7</td>
<td>Intelligenzstörung</td>
<td>−42,20</td>
</tr>
<tr>
<td>F8</td>
<td>Entwicklungsstörungen</td>
<td>68,76</td>
</tr>
<tr>
<td>F9</td>
<td>Verhaltens- und emotionale Störungen mit Beginn in Kindheit und Jugend</td>
<td>492,25</td>
</tr>
<tr>
<td>F90</td>
<td>Hyperkinetische Störungen</td>
<td>149,14</td>
</tr>
<tr>
<td>F91</td>
<td>Störungen des Sozialverhaltens</td>
<td>12,40</td>
</tr>
<tr>
<td>F92</td>
<td>Kombinierte Störungen des Sozialverhaltens und der Emotionen</td>
<td>15,75</td>
</tr>
<tr>
<td>F93</td>
<td>Emotionale Störungen des Kindesalters</td>
<td>86,67</td>
</tr>
<tr>
<td>F94</td>
<td>Störungen sozialer Funktion mit Beginn in Kindheit und Jugend</td>
<td>98,26</td>
</tr>
<tr>
<td>F95</td>
<td>Tic-Störungen</td>
<td>8,87</td>
</tr>
<tr>
<td>F96</td>
<td>Andere Verhaltens- und emotionale Störungen mit Beginn in Kindheit und Jugend</td>
<td>10,64</td>
</tr>
<tr>
<td>F99</td>
<td>Psychische Störung ohne nähere Angabe</td>
<td>0,75</td>
</tr>
</tbody>
</table>

### Tab. 3 Steigerung der Diagnosen der Kategorie F getrennt in den Jahren 2003 bis 2012 in den einzelnen Bundesländern

<table>
<thead>
<tr>
<th>Bundesland</th>
<th>Steigungscoefficient</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baden-Württemberg</td>
<td>90,12</td>
<td>&lt; 0,001</td>
</tr>
<tr>
<td>Bayern</td>
<td>121,68</td>
<td>0,001</td>
</tr>
<tr>
<td>Berlin</td>
<td>19,53</td>
<td>0,013</td>
</tr>
<tr>
<td>Bremen</td>
<td>0,80</td>
<td>0,892</td>
</tr>
<tr>
<td>Hamburg</td>
<td>60,85</td>
<td>&lt; 0,001</td>
</tr>
<tr>
<td>Hessen</td>
<td>54,71</td>
<td>0,006</td>
</tr>
<tr>
<td>Mecklenburg-Vorpommern</td>
<td>22,78</td>
<td>0,014</td>
</tr>
<tr>
<td>Niedersachsen</td>
<td>55,55</td>
<td>0,001</td>
</tr>
<tr>
<td>Nordrhein-Westfalen</td>
<td>250,74</td>
<td>&lt; 0,001</td>
</tr>
<tr>
<td>Rheinland-Pfalz</td>
<td>105,90</td>
<td>&lt; 0,001</td>
</tr>
<tr>
<td>Saarland</td>
<td>13,35</td>
<td>0,084</td>
</tr>
<tr>
<td>Sachsen</td>
<td>130,74</td>
<td>&lt; 0,001</td>
</tr>
<tr>
<td>Sachsen-Anhalt</td>
<td>30,69</td>
<td>0,071</td>
</tr>
<tr>
<td>Schleswig-Holstein</td>
<td>13,16</td>
<td>0,156</td>
</tr>
<tr>
<td>Thüringen</td>
<td>8,22</td>
<td>0,001</td>
</tr>
</tbody>
</table>
sen (z. B. Störungen des Autismusspektrums, Tic-Störungen) (10). Interessant scheint in diesen Zusammenhang, dass die aktuelle Welle 1 der KiGGS-Studie im Studienzeitraum zwar keine Zunahme an psychischen und Verhaltensstörungen in der Allgemeinbevölkerung beschrieben hat (9), doch sowohl die ambulante psychotherapeutische, medikamentöse als auch die stationäre Behandlung zugenommen haben.

Besonders kritisch in diesem Zusammenhang ist die Zunahme der Pharmakotherapien zu bewerten, die sich im vergleichbaren Beobachtungszeitraum zeigen ließ (2).


Ein weiteres interessantes Ergebnis ist ein ähnlicher Anstieg in stationär behandelten Kindern und Jugendlichen in den alten und neuen Bundesländern. Laut KiGGS sind wahrscheinlich 9,9% der Kinder in den alten und 8,7% in den neuen Bundesländern psychisch auffällig (15).


Folglic scheint der Versorgungslücke in Deutschland mit einer zunehmenden Anzahl an ambulanten und stationären Behandlungen begegnet worden zu sein. Das kann als verbesserte Versorgung psychisch kranker Kinder und Jugendlicher interpretiert werden. Dennoch verdeutlichen die Faktoren langen Wartelisten, dass das Versorgungsangebot noch immer nicht die Inanspruchnahme deckt (6). Hier drängt sich die Notwendigkeit des weiteren Ausbaus der Kapazitäten auf. Dabei sollte der demographische Wanderungsbereich berücksichtigt werden. Für die kommenden Jahre wird eine rückläufige Zahl der von psychischen und Verhaltensstörungen stationär behandelten Patienten prognostiziert, weil die Anzahl an Kindern und Jugendlichen voranschreitend abnimmt und die der 60- bis 80-Jährigen zunehmen wird. Psychische und Verhaltensstörungen sind bei den Hochbetagten mit 16% geringer als bei ihrer Bevölkerungsanteil (20%) entspricht. Bis 2030 soll sich die Anzahl sogar um 10,8% reduziert haben (16).

**Fazit**


**Limitation**


**Interessenkonflikt**


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Suicidal behavior in German adolescents: prevalence and association with depressive and manic symptoms

6.2 Suicidal behavior in German adolescents: prevalence and association with depressive and manic symptoms

J. Straub’s contribution to the article:
J. Straub generated the data matrix, did data input, executed statistical analyses, and interpreted statistical outcomes. She researched literature, wrote the manuscript, integrated remarks of the co-authors, revised the manuscript according to reviewer’s comments, and created figures and tables.

Co-authors’ contributions to the article:
F. Keller assisted in statistical analyses. P.L. Plener conceptualised the study, coordinated its procedure, and did data acquisition. All co-authors reviewed the draft and gave constructive remarks.

Reference

Suicidal Behavior in German Adolescents
Prevalence and Association with Depressive and Manic Symptoms

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Abstract. Objective: Research in adults has identified an association between bipolar disorder and suicidal behavior. This relationship, however, has been insufficiently investigated in adolescents to date. Methods: 1,117 adolescents from 13 German schools (mean age = 14.83, SD = .63; 52.7% females) completed an extended German version of the Center for Epidemiological Studies Depression Scale (CES-D), which assesses depressive and manic symptoms during the last week, as well as the Self-Harm Behavior Questionnaire (SHBQ) for the assessment of lifetime suicidal behavior. Results: In the present sample 39.4% of the girls and 23.1% of the boys reported lifetime suicidal thoughts and 7.1% of the girls as well as 3.9% of the boys a lifetime history of suicide attempts. 18.7% of the adolescent sample revealed elevated symptoms of depression and 9% elevated levels of mania symptoms. Elevated sum scores of depression and mania were associated with a higher number of suicidal ideations and suicide attempts. A block-wise regression analysis revealed that sum scores of depression and mania predicted suicidal ideations best. Concerning suicide attempts, the best predictors were age as well as depression and mania sum scores. Conclusions: Suicidal behavior was reported more often when adolescents demonstrate symptoms of mania as well as symptoms of depression than when they demonstrate only depressive symptoms. The presence of bipolar symptoms in adolescents should alert clinicians to the heightened possibility of suicidal behavior.

Keywords: depression, mania, bipolar disorder, adolescents, suicidal behavior

Suizidales Verhalten bei Jugendlichen in Deutschland – Prävalenz und Zusammenhang mit depressiven und manischen Symptomen


Schlüsselwörter: Depression, Manie, bipolare Störung, Jugendliche, suizidales Verhalten

Introduction

Suicide is the second most leading cause of death among children and adolescents in Europe. Male adolescents commit suicide nearly four times more often than female adolescents (Värnik et al., 2009), whereas suicidal ideations and suicide attempts are more prevalent in adolescent females (Kokkevi, Rotsika, Arapaki, & Richardson, 2012). The median lifetime prevalence rate for suicide attempts in adolescents from 17 European countries (15–16 years old) was reported to be 10.5%. Prevalence rates in Germany are slightly lower and range from 6.5 to 7.9% (Plener, Fegert, & Koelch, 2012). Suicidal behavior is often related to affective disorders, such as depression and bipolar disorder.
(Allison, Roeger, Martin, & Keeves, 2001; Brent et al., 1993). Bipolar disorder emerges in prepubescent children and adolescents, demonstrating a lifetime prevalence of 2.1% among 15–18-year-olds (Kozloff et al., 2010). Early onset of bipolar disorder coincides with a negative long-term prognosis for comorbid diagnoses and an elevated risk for suicide (Azorin et al., 2010; Van Meter, Moreira, & Youngstrom, 2011). In a large study with adolescents from the United States, Nock et al. (2013) demonstrated that 56.8% of adolescent suicide ideators suffered from major depressive disorder (MDD) or dysthymia and 9.1% from bipolar disorders. Furthermore, 75.7% of suicide attempters suffered from MDD or dysthymia and 13.2% of bipolar disorder. Lifetime prevalence rate for at least one suicide attempt of adolescents suffering from bipolar disorders of other studies, range from 32% (Goldstein et al., 2005) to 44% (Lewinsohn, Seeley, & Klein, 2003), and retrospective analysis of adolescent suicide completers revealed that 46.3% fulfilled criteria for lifetime diagnoses of MDD and 17.9% for bipolar spectrum disorder (Brent et al., 1993).

Evidence providing population-based numbers for the German population is scarce, so that there is still a need for comparable studies from Germany. The present study aimed to explore (1) the prevalence rate of suicidal behavior, (2) depressive and manic symptoms in a German adolescent school sample, and (3) the relationship between depressive/manic symptoms and suicidal behavior. We were also interested to discover (4) whether depressive/manic symptoms predict suicidal behavior and (5) whether certain groups of symptoms of the mania scale predict suicidal behavior better than others.

### Methods

#### Participants

Adolescents from the ninth grades (N = 1,117) of 13 schools in southern Germany participated in an anonymous assessment. The adolescents were between the age of 14 and 17 (M = 14.83; SD = .63); 52.7% were female and 47.3% male. With regard to three types of secondary schools that are available in Germany, 469 (42%) were attending a Gymnasium, 492 (44%) a Realschule, and 156 (14%) a Hauptschule. Written informed consents, both by the students and their caregivers, were obtained before data collection, and approval was given by the regional council, the local education authority, and the principals of the schools. The study was approved by the IRB of the University of Ulm. Due to regulations of the school authorities, no data could be obtained from nonparticipating students.

#### Diagnostic Instruments

The Centre for Epidemiological Studies Depression Scale (CES-D) (Radloff, 1977) is a frequently used instrument for the assessment of depressive symptoms in the general population. It has been translated into the German version Allgemeine Depressionsskala (ADS; Hautzinger, Bailer, Hofmeister & Keller, 2012; Hautzinger & Bailer, 1993), which consists of 20 items assessing depressive symptoms during the previous week (item values range from 0–3), with an internal consistency of .85 (Meyer & Hautzinger, 2001). A score above 22 indicates an elevated risk of depression (Hautzinger et al., 2012) and Cronbach’s α of the present sample was .87.

Table 1

<table>
<thead>
<tr>
<th>Items</th>
<th>Suicidal ideations</th>
<th>Suicide attempts</th>
</tr>
</thead>
<tbody>
<tr>
<td>21 Elevated mood (EMIS)</td>
<td>.07*</td>
<td>.06</td>
</tr>
<tr>
<td>22 Thoughts are racing (IDCA)</td>
<td>.23***</td>
<td>.17***</td>
</tr>
<tr>
<td>23 Irritability (IDCA)</td>
<td>.31***</td>
<td>.18***</td>
</tr>
<tr>
<td>24 Increase in goal-directed activity (EMIS)</td>
<td>.06</td>
<td>.02</td>
</tr>
<tr>
<td>25 Distractibility (IDCA)</td>
<td>.29***</td>
<td>.12***</td>
</tr>
<tr>
<td>26 Decreased need for sleep</td>
<td>.03</td>
<td>.07*</td>
</tr>
<tr>
<td>27 More talkative than normal</td>
<td>.13***</td>
<td>.05</td>
</tr>
<tr>
<td>28 Inflated self-esteem or grandiosity (EMIS)</td>
<td>.08*</td>
<td>.06</td>
</tr>
<tr>
<td>29 Psychomotor agitation</td>
<td>.21***</td>
<td>.09**</td>
</tr>
<tr>
<td>IDCA</td>
<td>.37***</td>
<td>.21***</td>
</tr>
<tr>
<td>EMIS</td>
<td>.03</td>
<td>.04</td>
</tr>
</tbody>
</table>

Note. *p < .05, **p < .01, ***p < .001. Factor attributions in parentheses: IDCA = irritability and disturbed cognitive abilities; EMIS = elevated mood and inflated self-esteem.

The ADS has been extended using nine questions (for item content of the mania subscale see Table 1; item values range from 0–3) to cover DSM-IV criteria for a hypomania/mania episode (internal consistency of .64) by Meyer and Hautzinger (2001). Examples for items are “During the last week I was unusually happy, aroused or hyped up” and “During the last week I was extremely active and busy with lots of things.” In our study Cronbach’s α was .65 for the mania subscale. No cutoff has been established for the mania subscale so far, but mean scores equal and above 12 (85 percentile) (Meyer & Hautzinger, 2001) can be interpreted as elevated values or sub threshold values.

Suicidal behavior was assessed by means of the Self-Harm Behavior Questionnaire (SHBQ) (Gutierrez, Osman, Barrios & Kopper, 2001), which is a 34-item questionnaire assessing lifetime self-harm behavior, suicidal ideations, and attempts. The German version demonstrated a high internal consistency (Cronbach’s α = .87–.96), good interrater reliability (r = .87) and satisfying test–retest reliability (3 days: r = .65). Furthermore concordance with a different self-report questionnaire that assesses self-harm as well, was good (K = .63, ICC = .79) providing evidence for convergent validity. Correlations between clinician rating and SHBQ however was low (K = .22, ICC = .34) (Fliege et
al., 2006). Muehlenkamp, Cowles, and Gutierrez (2010) demonstrated that the four-factor structure of the SHBQ is robust, and convergent validity was moderate. The questions used for the assessment of suicidal behavior were, “Have you ever attempted suicide?” and “Have you ever thought about committing suicide?”

**Factors of the Mania Subscale**

To determine factors of the mania subscale the scree-test and parallel analysis criteria were applied, and calculations were done using O’Connor (2000)’s program. This was done to better understand which groups of items are especially suitable to predict suicidal behavior.

A factor analysis of the mania subscale revealed eigenvalues of 2.45 and 1.30; all other values were < 1. According to the parallel-analysis criterion, the random value of the second eigenvalue was 1.13 (95%), which was exceeded by the second eigenvalue. Thus, it was assumed that the mania subscale compasses two factors: The first factor includes items 22, 23, and 25 and can be summarized as “irritability and disturbed cognitive abilities” (IDCA); the second factor includes items 21, 24, and 28 (see Table 1 for items) and can be best described as “elevated mood and inflated self-esteem” (EMIS). The remaining three items had similar loadings on both factors and could not be attributed clearly.

**Statistical Methods**

Differences between scores of depression and mania items in students reporting suicidal ideations or suicide attempts and in those who didn’t as well as age effects on depression and manic symptoms were calculated by means of t-tests, and associations were calculated by means of the Pearson correlation coefficient. Differences between age groups concerning suicidal behavior were calculated by means of χ² test. Furthermore, we ran a logistic regression with block-wise entry method. In a first block we entered the covariates age and sex. In a second block we entered the depression sum score. In a third block we either entered the mania sum score or both mania factors EMIS and IDCA instead. Statistical analyses were performed using PASW statistics 18 and SAS 9.3 software.

**Results**

**Prevalence of Suicidal Behavior**

Suicidal ideations in the past were reported by 31.8% of the adolescents. Split according to sex, 39.4% of the girls and 23.1% of boys reported previous suicidal thoughts. Furthermore, a total of 5.6% (7.1% of the girls and 3.9% of the boys) reported having attempted suicide in the past. 1.7% reported suicide attempts within the last year, which constituted 34.5% of all attempts. Of those who reported suicide attempts in the past, 73.3% also reported having had prior suicidal ideations. Of those who reported suicidal ideations, 13.3% reported suicide attempts as well, whereas only 2.3% reported suicide attempts without having had any previous suicidal ideations. The number of suicide attempts (χ² (2) = 16.12, p = .001) increased by age especially between the age of 15 and 16 (see Table 2), and suicidal ideations rose as well by age albeit not significantly (χ² (2) = 4.77, p = .09).

**Mania and Depression Scores**

The prevalence rate for elevated symptoms of depression amounted to 18.7% (27% of the girls and 9.5% of boys) in the present sample and the mean value of the depression subscale was 15.02 (SD = 9.54). The latter was significantly higher in girls (M = 17.86, SD = 9.92) than in boys (M = 11.82, SD = 7.96; t(1070) = 11.10, p < .001). Between the age of 14 (M = 14.08, SD = 9.16) and 15 (M = 15.05, SD = 9.48) depression scores were comparable (t(968) = –1.52, p = .13). In comparisons of adolescents of 14 and 16 years (M = 17.26, SD = 10.55) of age (t(410) = –2.90, p = .004) as well as 15 and 16 years of age, depression scores differed significantly (t(752) = –2.12, p = .04).

### Table 2

**Prevalence rates for elevated depression and mania symptoms as well as suicidal ideations and attempts for boys and girls between 14 and 16 years of age**

<table>
<thead>
<tr>
<th></th>
<th>Age of 14 (N = 321)</th>
<th>Age of 15 (N = 679)</th>
<th>Age of 16 (N = 102)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Prevalence rate</td>
<td>Prevalence rate girls</td>
<td>Prevalence rate boys</td>
</tr>
<tr>
<td>Depression</td>
<td>18.1%</td>
<td>27.3%</td>
<td>7.4%</td>
</tr>
<tr>
<td>Mania</td>
<td>7.5%</td>
<td>8.7%</td>
<td>6.0%</td>
</tr>
<tr>
<td>Suicidal ideations</td>
<td>27.6%</td>
<td>34.3%</td>
<td>19.7%</td>
</tr>
<tr>
<td>Suicide attempts</td>
<td>3.8%</td>
<td>5.3%</td>
<td>2.0%</td>
</tr>
</tbody>
</table>

**Note.** N = number of participants; prevalence rates split per sex were calculated in relation to their particular sex e.g., 27.3% of 14-year-old girls in relation to all 14-year-old girls had elevated depression scores. Scores above 22 in the ADS indicate an elevated risk for depression. Scores above 12 in the extended version of the ADS indicate elevated hypomania/mania symptoms.
The prevalence rate for an elevated level of mania symptoms amounted to 9% (9% of the girls and 9.1% in boys) in the present sample, and the mean value of the mania subscale was 5.87 (SD = 3.9). The mean value of manic scores was again higher in girls (M = 6.22, SD = 3.78) than in boys (M = 5.47, SD = 4.00; t(1080) = 3.17, p < .01). The mania scores did not differ between 14- (M = 5.61, SD = 3.80) and 15-year-olds (M = 5.87, SD = 3.90; t(968) = −1.00, p = .32) and 15- and 16-year-olds (M = 6.59, SD = 4.35) of age (t(752) = −1.68, p = .09), but did differ between 14- and 16-year-old students (t(146) = −2.02, p = .05).

Mania and Depression Scores and Suicidal Behavior

The mean sum score of depression was significantly higher (t(479.94) = −15.66, p < .001) in those who reported previous suicidal ideations (M = 21.92, SD = 10.56) compared to those who never thought about suicide (M = 11.90, SD = 7.12). Furthermore, those with a history of suicide attempts showed a significantly higher mean sum score of depression (M = 25.75, SD = 10.83) than those without a history of suicide attempts (M = 14.42, SD = 9.14; t(62.96) = −7.87, p < .001).

Adolescents with a history of suicidal ideations had significantly higher (t(563.08) = 8.66, p < .001) mean sum scores in the mania subscale (M = 7.49, SD = 4.16) than those without a history of suicide attempts (M = 5.2, SD = 3.50). The mean sum score of the mania subscale in students with previous suicide attempts (M = 8.53, SD = 4.11) was significantly higher (t(1058) = −5.48, p < .001) than in those without previous suicide attempts (M = 5.71, SD = 3.81). The factor “IDCA” correlated significantly with suicide attempts and suicidal ideations, whereas “EMIS” correlated with none of them. The item “psychomotor agitation,” which loaded on both factors, was also correlated significantly with suicidal ideations and suicide attempts. For further correlations between single mania items and suicide attempts as well as suicidal ideations see Table 1.

14.3% of the adolescents with elevated mania sum scores (N = 98) reported previous suicide attempts compared to 16.9% of those with elevated depression sum scores (N = 207). The highest prevalence rate for suicide attempts of 20% was found in adolescents who reported both elevated mania and depression sum scores (N = 40).

Table 3
Depression sum scores and mania factors as predictors for suicidal ideations and attempts

<table>
<thead>
<tr>
<th>Suicidal ideations</th>
<th>Block 1</th>
<th>Block 2</th>
<th>Block 3a</th>
<th>Block 3b</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B</td>
<td>SE</td>
<td>WALD</td>
<td>p-value</td>
</tr>
<tr>
<td>Block 1 Age</td>
<td>.09</td>
<td>.12</td>
<td>.48</td>
<td>.49</td>
</tr>
<tr>
<td>Sex</td>
<td>−1.11</td>
<td>.16</td>
<td>.46</td>
<td>.50</td>
</tr>
<tr>
<td>Block 2 Sum score depression</td>
<td>.12</td>
<td>.01</td>
<td>99.02</td>
<td>.00</td>
</tr>
<tr>
<td>Block 3a Sum score mania</td>
<td>.09</td>
<td>.02</td>
<td>20.78</td>
<td>.00</td>
</tr>
<tr>
<td>Block 3b IDCA</td>
<td>.10</td>
<td>.05</td>
<td>4.72</td>
<td>.03</td>
</tr>
<tr>
<td>EMIS</td>
<td>.14</td>
<td>.04</td>
<td>10.15</td>
<td>.00</td>
</tr>
<tr>
<td>Constant</td>
<td>−4.32</td>
<td>1.85</td>
<td>5.48</td>
<td>.02</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Suicide attempts</th>
<th>Block 1</th>
<th>Block 2</th>
<th>Block 3a</th>
<th>Block 3b</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B</td>
<td>SE</td>
<td>WALD</td>
<td>p-value</td>
</tr>
<tr>
<td>Block 1 Age</td>
<td>.56</td>
<td>.21</td>
<td>7.27</td>
<td>.01</td>
</tr>
<tr>
<td>Sex</td>
<td>−.07</td>
<td>.31</td>
<td>.05</td>
<td>.83</td>
</tr>
<tr>
<td>Block 2 Sum score depression</td>
<td>.08</td>
<td>.02</td>
<td>23.97</td>
<td>.00</td>
</tr>
<tr>
<td>Block 3a Sum score mania</td>
<td>.09</td>
<td>.04</td>
<td>6.55</td>
<td>.01</td>
</tr>
<tr>
<td>Block 3b IDCA</td>
<td>.10</td>
<td>.08</td>
<td>1.55</td>
<td>.21</td>
</tr>
<tr>
<td>EMIS</td>
<td>.16</td>
<td>.07</td>
<td>4.86</td>
<td>.03</td>
</tr>
<tr>
<td>Constant</td>
<td>−13.33</td>
<td>3.15</td>
<td>17.91</td>
<td>.00</td>
</tr>
</tbody>
</table>

Note. B = regression coefficient; SE = standard error; OR = odds ratio. Suicidal ideations model: R² = .24 (Cox & Snell), .33 (Nagelkerke). Model χ² (5) = 273.60, p < .001; Suicide attempts model: R² = .07 (Cox & Snell), .20 (Nagelkerke). Model χ² (5) = 75.86, p < .001.

Prediction of Suicidal Behavior

Logistic regression analysis revealed that both the sum scores of depression and mania were significant predictors for suicidal ideations after controlling for age and sex, both of which were nonsignificantly related to suicidal ideations. If we include both factors of the mania subscale instead of the mania sum score, suicidal ideations were predicted by both mania factors IDCA and EMIS. Age and the sum score of depression were significant predictors with respect to suicide attempts. After controlling for these predictors, we found that the mania sum score was of additional predictive value. After replacing the mania sum score by the two mania factors, suicide attempts were predicted only by the factor EMIS (see Table 3). In addition, suicide attempts were predicted by suicidal ideations and age as well (see Table 4).
Table 4

Predictors of suicide attempts

<table>
<thead>
<tr>
<th>Suicide attempts</th>
<th>B</th>
<th>SE</th>
<th>WALD</th>
<th>p-value</th>
<th>95% CL for odds ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>.66</td>
<td>.21</td>
<td>10.24</td>
<td>.001</td>
<td>1.29</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
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<td>1.94</td>
</tr>
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<td></td>
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<td></td>
<td></td>
<td>2.91</td>
</tr>
<tr>
<td>Sex</td>
<td>.24</td>
<td>.29</td>
<td>.67</td>
<td>.41</td>
<td>.72</td>
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<td>1.27</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2.26</td>
</tr>
<tr>
<td>Suicidal ideations</td>
<td>−1.81</td>
<td>.31</td>
<td>35.04</td>
<td>.00</td>
<td>.09</td>
</tr>
<tr>
<td></td>
<td></td>
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<td>.16</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>.30</td>
</tr>
<tr>
<td>Constant</td>
<td>−11.94</td>
<td>3.12</td>
<td>14.63</td>
<td>.00</td>
<td>.00</td>
</tr>
</tbody>
</table>

Note. B = regression coefficient; SE = standard error; OR = odds ratio. \( R^2 = .05 \) (Cox & Snell), .15 (Nagelkerke); Model \( \chi^2 (3) = 56.93, p < .001 \).

Discussion

The present study assessed the prevalence rates of lifetime suicidal ideations and suicide attempts as well as the prevalence rates for elevated depressive and mania symptoms in an adolescent sample. Furthermore, we were interested in associations between elevated symptoms and suicidal behavior as well as predictors of suicidal behavior. Our results demonstrate that nearly 19% of the adolescents revealed elevated symptoms of depression and 9% showed elevated symptoms of mania. Nearly 32% of adolescents reported suicidal ideations in the past and 5.6% suicide attempts. Depression and mania sum scores were associated with suicidal ideations, and both sum scores as well as age were associated with suicide attempts.

The mean lifetime prevalence rate for suicidal ideations in our study was 31.8% (39.4% of the girls and 23.1% of the boys). Those findings are comparable to the results of a systematic review, comprising 128 studies with adolescents who reported a lifetime prevalence rate for suicidal thoughts of 29.9% (95% CI, 26.1–33.8) (Evans, Hawton, Rodham, Psychol & Deeks, 2005). Furthermore, the prevalence rate of the present study seems to lie within the international range of 15- to 16-year-olds, which ranges from 15% in Armenia to 43.8% in Latvia (Kokkevi et al., 2012). In our sample, the prevalence rate for suicide attempts was 5.6% (7.1% of the girls and 3.9% of the boys), which lies at the lower end of the lifetime prevalence rates reported from the crossnational comparison of Kokkevi et al. (2012), which ranged from 4.1% in Armenia to 23.5% in Hungary. The systematic review of Evans et al. (2005) revealed that, on average, 9.7% of adolescents reported to have attempted suicide at least once in their life, which is higher than the findings in our sample. This could be explained by the fact that the age-span in the review of Evans et al. was between 12 and 20 years of age, and the authors found that prevalence rates were lower in European samples than, for example, in American samples.

Concerning effects of sex, Kokkevi et al. (2012) found that females revealed double the number of suicidal ideations and suicide attempts of males. Evans et al. (2005) also found that the rates of suicidal thoughts were at least 1.25 times higher and suicide attempts more than twice that of males. In the present study, females show 1.7 times higher rates of suicidal ideations and attempts than males. In our study, suicidal thoughts and age were significant predictors for suicide attempts which was also shown by Kokkevi et al. (2012).

The mean prevalence rate for depressive symptoms was 18.7% in our sample. Split by sex, 27% of the girls and 9.5% of the boys reported having depressive symptoms during the last week. Those results are comparable to those of Allison et al. (2001), who found prevalence rates of 21.4% for girls and 13.2% for boys; and of Bettge et al. (2008), who found prevalence rates of 21.2% for girls and 12.3% for boys. In summary, the depression scores for females seem to be slightly higher in our sample than in other studies, which again could be explained by the fact that Bettge et al. (2008) and Allison et al. (2001) included younger adolescents than we did. With respect to age effects Bettge et al. (2008) found – comparable to our results – that older adolescents reported higher depression scores. The mean value of 15.02 in the ADS was within the range [12.5–16.98] found in other studies (Allison et al., 2001). Scores in the ADS were higher in females than in males, something also confirmed by Allison et al. (2001).

If we consider subthreshold values in the ADS extended mania subscale (Meyer & Hautzinger, 2001), 9% of the adolescents in our sample revealed elevated symptoms. Angst et al. (2010) demonstrated that patients with threshold hypomania in addition to depression differ from patients with major depression alone through their elevated tendency toward suicide attempts. This is in line with our finding that 20% of the adolescents with elevated mania and depression scores reported previous suicide attempts. The result is comparable to that of Strober et al. (1995), who found a 5-year prospective prevalence rate of 20% in adolescents with bipolar disorders, which is slightly lower than the association between lifetime bipolar disorders and suicide attempts (13.2%) reported by Nock et al. (2013). Furthermore, prevalence rates for subthreshold mania symptoms in our sample were comparable between the sexes, which was also found in hospitalized adolescents with manic and mixed episodes (Brunelle et al., 2009).

In the present study, depression and mania sum scores best predicted suicidal ideations. Depression and mania...
sum scores as well as age predicted suicide attempts. Those results show a different picture than in the study of Nock and colleagues (2009), who stated that depression alone is the best predictor for suicidal ideations and bipolar disorder is one of the best predictors for unplanned suicide attempts. Contrary to our findings, Resch et al. (2008) found age effects on both suicidal ideations and attempts. One explanation for the different outcomes could be the large age-span ranging from 11 to 17 years.

Under closer consideration of the mania symptoms, suicidal ideations were significantly predicted by both mania factors of the extended version of the ADS, whereas suicide attempts were predicted only by the mania-factor “elevated mood and inflated self-esteem (EMIS).” This may be attributed to a heightened frustration because of the discrepancy between an initial highly positive state, which is often followed by a subsequent depressive phase.

Our study has several limitations that need to be considered. The extended version of the ADS assesses symptoms of depression and mania occurring during the preceding week. Therefore, memory bias is expected to be weak. But we didn’t collect information about the course preceding week. Therefore, memory bias is expected to be significant. But we didn’t collect information about the course preceding week. Therefore, memory bias is expected to be significant. This may be attributed to a heightened frustration because of the discrepancy between an initial highly positive state, which is often followed by a subsequent depressive phase.

In addition, self-reports instead of clinical interviews were used to assess depressive and manic symptoms. Furthermore, we defined depression and mania sum scores as predictor variables for suicidal ideations and attempts, although the causality is not clear. In addition, it remains unsolved whether mania symptoms in adolescents are clearly distinguishable from ADHD and depressive disorders in adolescents, an aspect frequently discussed in the literature (Meyer & Hautzinger, 2001; Meyer, Kößmann-Boehm, & Schlottke, 2004). Finally, it needs to be pointed out that explained variance in regression analysis as well as correlation coefficients were small. Furthermore, the mania factor “EMIS” was insignificantly correlated but still a significant predictor for suicidal ideations and suicide attempts in the combination with other predictors in the regression analyses.

This study points to the added value of specifically exploring symptoms of mania in addition to symptoms of depression when assessing suicidal behavior in adolescents – an aspect often neglected in children and adolescents because of its low prevalence rate. If we take a more detailed look at the mania scale, the factor EMIS, which describes elevated mood and inflated self-esteem, becomes a significant predictor for suicidal ideations and suicide attempts and the factor IDCA, which describes irritability and disturbed cognitive abilities for suicidal ideations. The clinician should also be alerted when patients demonstrate psychomotor agitation as this item was also significantly associated with suicidal behavior.

References


adolescents and young adults: Results from an epidemiological sample. *Journal of Affective Disorders*, 125, 350–354.


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Conflicts of interest:
J. Straub declares no conflict of interest.
F. Keller declares no conflict of interest.
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M. G. Koelch declares no conflict of interest. He received unrestricted grants from Eli Lilly International Foundation. He got research grants from the BMFFSJ (German Ministries for Family Affairs, Senior Citizens, Women and Youth), the BMBF (German Ministries for Research and Education), the Schweizer Bundesamt für Justiz and from Boehringer-Ingelheim. He was CI or PI for Eli Lilly, Astra Zeneca and Janssen-Cilag, Lundbeck. He received travel grants or payments for lectures from Janssen-Cilag, the University of Rostock, DGKJP, UCB, Europäische Akademie and from various nonprofit organizations. He isn’t stockholder or share-holder in the pharmaceutical industry. P. Plener declares no conflict of interest. He is PI for Lundbeck. He got research grants from the BMBF (German Ministries for Research and Education) and the BfArM (German Federal Institute for Drugs and Medical devices). He received travel grants from the DFG, DAAD and IA-CAPAP. He is neither stockholder nor shareholder in the pharmaceutical industry.

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Convergence of children's depression rating scale-revised scores and clinical diagnosis in rating adolescent depressive symptomatology

6.3 Convergence of children's depression rating scale-revised scores and clinical diagnosis in rating adolescent depressive symptomatology

Main authors' contributions to the article:
P.L. Plener together with M.G. Koelch conceptualized the study, coordinated the study procedure, recruited the study participants, scheduled diagnostic appointments, and controlled return of diagnostic instruments. P.L. Plener managed data input, executed statistical analyses and interpreted statistical outcomes. He researched literature, wrote the manuscript, integrated remarks of the co-authors, and revised the manuscript according to reviewer’s comments.

Contributions of J. Straub and co-authors to the article:
We helped drafting and reviewing the manuscript and helped with revising the manuscript according to the reviewer’s comments.

Reference
Convergence of children's depression rating scale-revised scores and clinical diagnosis in rating adolescent depressive symptomatology

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Abstract

The Children’s Depression Rating Scale-Revised (CDRS-R) is a widely used instrument for research on depression in minors. A raw score of ≥40 has often been used as indicator of depressive symptomatology. As a validated German version of the CDRS-R has recently become available, we assessed CDRS-R raw summary scores of a video taped interview session in two different rater groups and compared them with clinical ratings of International Classification of Diseases (ICD-10) depression diagnosis as observed by a third independent group. We found that for the German version a raw score between 35 and 40 is indicative for mild depressive symptomatology as described by the ICD-10. CDRS-R scores show potential clinical applicability to deduce levels of depression.

Introduction

The Children’s Depression Rating Scale-Revised (CDRS-R) is nowadays one of the most frequently used instruments for the assessment of depressive symptomatology in minors in the context of clinical trials. It was originally intended as rating scale for the age group from 6 to 12 years, but is also widely used in adolescents.1 The CDRS-R is a clinician administered 17-item interview, with item ratings between 1 (=no difficulties) and 5 or 1 and 7 (=clinically significant difficulties) (adding up to a total score between 17 to 113). It has been proposed, that a score of ≥40 indicates depressive symptomatology, whereas a score ≤28 was often used as indicative of remission within trials.2 Good psychometric properties have been reported from the age group between 6 and 12 years (with an internal consistency of Cronbach’s α=0.85) as well as convergent validity with global depression rating (r=0.92).1 In a placebo controlled treatment study of 96 children (8-11 years) with fluoxetine, a Cronbach’s α of 0.86 was reported for the CDRS, as well as a correlation with the Montgomery-Asberg Depression Scale (MADRS)3 at baseline (r=0.51) and after the 9 weeks of the trial (r=0.85).4 Only recently, psychometric properties have been established in a sample of 145 adolescents with an age range between 12 and 18 years.2 The authors reported an excellent internal consistency of Cronbach’s α ranging between 0.79 and 0.92 for their three assessment waves (screening, baseline and exit). At the screening visit, the CDRS-R total score was significantly correlated with an major depressive disorder (MDD) diagnosis obtained from the Kiddie-Schedule for Affective Disorders and Schizophrenia-KSADS (K-SADS)2 (r=0.64; P<0.01). CDRS-R total scores were highly correlated with the Clinical Global Impression-Severity (CGI-S) at each of the three waves of the study (r=0.87, 0.80 and 0.93; P<0.01). Recently a German version of the CDRS-R was applied in 60 child and adolescent psychiatric inpatients (age range: 7.5-17.9 years),5 demonstrating good psychometric properties (internal consistency: Cronbach’s α=0.90) with high correlation with the Beck’s Depression Inventory II (German version by Hautzinger et al., 2006)7 in a subsample of 35 adolescents (r=0.79, P<0.001). In addition, the German version of the CDRS-R was also validated in a German child and adolescent (6.6 to 17.9 years) school population (n=275), showing good internal consistency (Cronbach’s α=0.86) as well, with a mean CDRS-R raw score of 25.18 (SD=7.96, range: 17-60).8

As up to now most of the literature available on the CDRS-R refers to US samples, thus comparing raw scores with Diagnostic and statistical manual of mental disorders, 4th ed., (DSM-IV) criteria for MDD, so far to our knowledge no study is available that compared CDRS-R scores with the clinical impression leading to International Classification of Diseases-10 diagnosis. As DSM-IV and International Classification of Diseases-10 (ICD-10) diagnostic criteria differ slightly, no information is available on how far CDRS-R scores offer information about the level of depressive symptomatology (mild, moderate or severe) of depressive episodes as defined by the ICD-10 (diagnosis of F32.0, F32.1 and F32.2 respectively). This is of relevance for establishing cut-off scores for future studies aiming to address mild to moderate forms of depressive symptomatology as defined in the ICD-10 and as treatment recommendations refer to the severity of depression, which is hardly assessed by assessment tools in clinical routine care.9

The aim of this study was to explore the convergence between raw scores of the CDRS-R and clinical diagnosis according to ICD-10.
Table 1. Professions and years of experience of the participants in the rating experiment. CDRS-R, Children’s Depression Rating Scale-Revised; ICD-10, International Classification of Diseases -10.

<table>
<thead>
<tr>
<th>Profession</th>
<th>n</th>
<th>Years of experience</th>
<th>Rating CDRS-R</th>
<th>Rating ICD-10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical student (8-11th term)</td>
<td>10</td>
<td>0</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Psychologist</td>
<td>2</td>
<td>0-10</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Child and Adolescent psychiatry resident</td>
<td>3</td>
<td>0-2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Pediatrices</td>
<td>2</td>
<td>1-4</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Psychotherapists in training</td>
<td>9</td>
<td>0-10</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Licensed psychotherapist</td>
<td>2</td>
<td>6</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Music therapist</td>
<td>2</td>
<td>5-9</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Child and Adolescent Psychiatry Consultant</td>
<td>2</td>
<td>5-12</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

Years of experience were not correlated with ICD-10 diagnostic level (Spearman’s \( \rho =0.34 \), n.s.)

Results

All participants handed back their CDRS-R scores (n=18) or their ICD-10 diagnosis (n=14) respectively. Clinical experience ranged between 0 and 12 years (mean: 3.05 years, SD: 4.07). 10 out of 32 participants were familiar with the CDRS-R.

CDRS-R mean raw score was 36.61 (SD: 5.07; range: 28-46; median: 35.5). The internal consistency was still satisfactory (Cronbach’s \( \alpha =0.71 \)), but lower than in the first sample and probably weakened by the two items without variance. Several items show medium to high values, while others were rated close to 1 and two items (4 and 7) were consistently rated with 1 (details on the CDRS-R items are provided in Table 2). Years of clinical experience were not significantly correlated with CDRS-R scores (Spearman’s \( \rho =-0.26 \), n.s.).

CGI-S mean score was 2.96 (SD: 1.0; range: 1-5), with years of clinical experience not being significantly correlated with CGI-S score (Spearman’s \( \rho =-0.02 \), n.s.). CGI-S score was correlated with CDRS-R raw score (Spearman’s \( \rho =0.55 \), \( P=0.04 \)).

Clinical ICD-10 diagnosis was rated by 14 participants and coded accordingly (0=no diagnosis of depression, 1=mild, 2=moderate, 3=severe depression). Out of the group, who rated clinically according to ICD-10, 5 participants (35.7%) rated no depression, 7 rated the case as mild depression (50%) and 2 (14.3%) rated it as moderate depression, with a mean score of 0.77 (SD=0.73; range: 0-2) being below the level of mild depression. CGI-S score was significantly correlated with severity of ICD-10 diagnosis (Spearman’s \( \rho =0.59 \), \( P=0.03 \)). Years of experience were not correlated with CDRS-R raw score (Spearman’s \( \rho =0.71 \), \( P=0.03 \)).

Discussion

We conducted a study on CDRS-R raw scores in relation to ICD-10 clinical diagnosis of depression to provide a comparison how clinical estimation of mild to moderate depression is correlated with scores of this frequently used assessment instruments. So far, a CDRS-R score of ≥40 was used as an indicator for depression in relation to DSM-IV MDD in several studies. As the distinction between mild, moderate and severe depression according to ICD-10 in relation to CDRS-R scores has so far not been established, we sought to determine a comparison based on a standardized video tape of an adolescent being interviewed using the CDRS-R. The mean raw scores of CDRS-R ratings of two independent rater groups were comparable (39.05 vs. 36.61 respectively), with the median scores even more closely comparable (37 vs 35.5). We found, that a CDRS-R raw score of approximately 37 points, was an indicator for a clinically derived diagnosis of mild to moderate depression in nearly 2/3 of the raters. The mean ratings for clinical diagnosis were slightly below the level of a mild depressive episode. We also sought for a diverse group of raters, finding, that the level of clinical experience did not affect the rating of the video tape. Based on our findings we would suggest, that a CDRS-R raw score band between 35 and 40 should be taken as indicative of mild to moderate depression according to the ICD-10. This may be of use to inform further studies using the CDRS-R as measure of depressive symptomatology. Limitations include the small size of the rater group, this approach didn’t deem to be feasible. Despite the abovementioned limitations, this is the first study to try to bridge the gap between scores as measured by a scientifically highly relevant research instrument and clinical diagnosis.

References

Agreement between self-report and clinician’s assessment in depressed adolescents, using the example of BDI-II and CDRS-R

6.4 Agreement between self-report and clinician’s assessment in depressed adolescents, using the example of BDI-II and CDRS-R

Contribution of J. Straub to the article:
J. Straub made decisions on the experimental design and conceptualized the study. She coordinated the study procedure, recruited study participants, and scheduled diagnostic appointments. She partially executed the diagnostic assessments. She generated the data matrix, did data input, executed statistical analyses, and interpreted statistical outcomes. She researched literature, wrote the manuscript, integrated remarks of the co-authors, revised the manuscript according to reviewer’s comments, and created figures and tables.

Co-authors’ contributions to the article:
F. Keller made decision on the experimental design and conceptualized the study. He helped with statistical analyses, interpreting the data, and writing and revising the manuscript according to the reviewer’s comments. P.L. Plener and M.G. Koelch reviewed the draft and gave constructive remarks. They helped with revising the manuscript according to the reviewer’s comments.

Reference

Konkordanz zwischen Selbst- und Klinikerurteil hinsichtlich depressiver Symptomatik bei Jugendlichen am Beispiel von BDI-II und CDRS-R

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Schlüsselwörter: Übereinstimmung von Selbst- und Fremdurteil, depressive Jugendliche, Korrelation auf Summenwerts-, Subskalen- und Einzelitemebene

Abstract. Agreement between self-report and clinician’s assessment in depressed adolescents, using the example of BDI-II and CDRS-R

Objectives: Preceding studies demonstrated a high agreement between self-report and clinician’s assessment of depression. The concordance on the level of sum scores, subscales, and single items, however, has yet to be investigated in a psychiatric adolescent sample. Also, the influence of additional variables such as age, sex, and IQ has been insufficiently studied in adolescents. Methods: Scores on the BDI-II and CDRS-R, assessed within 1 week, were collected from 105 adolescents (mean age = 15.94 years). Analyses of correlation were done on levels of sum scores, subscales, and single items. Results: There was a high correlation between self-report and clinician’s assessment (r = .67). At the level of subscales, items assessing somatic contents demonstrated no higher agreement than did items assessing cognitive and affective contents. The highest agreement at the symptom level was shown for the item assessing suicidal ideations. Additional variables had no significant influence on concordance. Adolescents with a high IQ and outpatient adolescents tended to overestimate their symptoms. Conclusions: The overall correlation was high and did not differ from results of comparable studies of correlations. The highest congruence was shown for the item assessing suicidal ideations, which underlines the accurate assessment of suicidality by clinicians as well. In summary, questionnaires can provide information about the existence of a depressive disorder, although one diagnostic instrument should not be replaced by the other despite a high correlation.

Keywords: Beck Depression Inventory – BDI-II, Children’s Depression Rating Scale, Revised (CDRS-R), concordance between self-report and clinician’s assessment, depressive adolescents, correlations
Einleitung


Neben diesen spezifischen Instrumenten sind noch klinische Interviews zu nennen, welche die Diagnostik psychischer Störungen im Allgemeinen – darunter auch Depressionen – ermöglichen: Kiddie-Sads Present and lifetime version (K-SADS-PL; Kaufman, Birmaher & Brent, 1997); klinisches Interview bei psychischen Störungen im Kindes- und Jugendalter (Kinder-Dips; Schneider, Unnewehr & Margraf, 2009).


Weiterhin könnten sich Drittvariablen, wie die Art der Depression oder das Vorliegen einer komorbiden psychischen Störung, auf den Zusammenhang zwischen Selbst- und Klinikerurteil auswirken (Corruble et al., 1999; Dorz, Borgherini, Conforti, Scarso & Magni, 2004). Bezüglich


Methoden

Teilnehmer


Tabelle 1

<table>
<thead>
<tr>
<th>Depressionsdiagnosen und Komorbiditäten der Teilnehmer laut ICD-10</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Depressive Störung</strong></td>
</tr>
<tr>
<td>F32.0 Leichte depressive Episode (N = 25)</td>
</tr>
<tr>
<td>F32.1 Mittelgradig depressive Episode (N = 56)</td>
</tr>
<tr>
<td>F32.2 Schwere depressive Episode (N = 11)</td>
</tr>
<tr>
<td>F32.3 Schwere depressive Episode mit psychot. Sympt. (N = 2)</td>
</tr>
<tr>
<td>F33.0 Rez. depressive Störung (leichte Episode) (N = 3)</td>
</tr>
<tr>
<td>F33.1 Rez. depressive Störung (mittelgradige Episode) (N = 1)</td>
</tr>
<tr>
<td>F33.2 Rez. depressive Störung (schwere Episode) (N = 1)</td>
</tr>
<tr>
<td>F33.3 Rez. depressive Störung (schwere Episode mit psychot. Sympt.) (N = 1)</td>
</tr>
<tr>
<td>F92.1 SSV mit depressiver Störung (N = 5)</td>
</tr>
</tbody>
</table>

Anmerkungen: N = Anzahl; SSV = Störung des Sozialverhaltens; rez. = rezidivierend.
Von den 105 Jugendlichen waren 77 (73.31 %) weiblich und 28 (26.66 %) männlich. Die Altersspanne reichte von 12.51 bis 18.97 Jahren \((M \pm SD = 15.94 \pm 1.63)\). 88 befanden sich in ambulanter und 17 in stationärer Behandlung. Von ihnen be- suchten 15.7 % die Mittelschule, 34.5 % die Realschule, 32.2 % das Gymnasium und 17.6 % befanden sich in einem Ausbildungsverhältnis. Der IQ reichte von 73 bis 129 \((M \pm SD = 103.51 \pm 10.85)\). Über die Hälfte der Teilnehmer (48.57 %) erfüllte die Kriterien für eine komorbide Störung (Tab. 1).

**Instrumente**


Beim der CDRS-R handelt es sich um ein semi-strukturiertes klinisches Interview, das auf den DSM-IV Kriterien zur Erfassung von Depressionen beruht und in Anlehnung an die HAM-D entwickelt wurde. Die CDRS-R wurde ursprünglich in den 70er-Jahren im amerikanischen Sprachraum entwickelt, in den 80er-Jahren überarbeitet (Poznanski & Mokros, 1996) und ist seit 2012 auch als deutsche Version erhältlich (Keller et al., 2012). Sie besteht aus insgesamt 17 Items, wovon 3 Items nonverbale Sym- tome, wie beispielsweise den mimischen Ausdruck, erfassen. Insgesamt konnten gute psychometrische Eigenschaf- ten wie eine hohe interne Konsistenz \((\alpha = 0.85)\), gute Trennschärfe- koefﬁzienten für die einzelnen Items sowie eine gute Test-Retest Reliabilität nach einer Woche \((r = 0.92)\) sowie Interrater-Re- liabilität \((r = 0.95)\) belegt werden (Keller et al., 2012).


**Statistische Analysen**


**Ergebnisse**

Durchschnittlich hatten die Jugendlichen im BDI-II einen Mittelwert von 24.76 \((SD = 11.87)\) und in der CDRS-R einen Mittelwert von 51.63 \((SD = 13.99)\). Mädchen wiesen...
### Tabelle 2

**Korrelation der CDRS-R Faktoren und BDI-II Faktoren**

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Anhedonie</td>
<td>.48</td>
<td>.06</td>
<td>.15</td>
<td>.24</td>
<td>.23</td>
<td>.68</td>
</tr>
<tr>
<td>Gedanken an den Tod</td>
<td>.06</td>
<td>.10</td>
<td>.31</td>
<td>.48</td>
<td>.35</td>
<td>.44</td>
</tr>
<tr>
<td>Körperl. Beschwerden</td>
<td>.15</td>
<td>.31</td>
<td>.37</td>
<td>.44</td>
<td>.53</td>
<td>.54</td>
</tr>
<tr>
<td>Berichtete depr. Stimmung</td>
<td>.24</td>
<td>.48</td>
<td>.44</td>
<td>.46</td>
<td>.53</td>
<td>.54</td>
</tr>
<tr>
<td>Somatisch-affektiv (BDI-II)</td>
<td>.09</td>
<td>.40</td>
<td>.31</td>
<td>.53</td>
<td>.54</td>
<td>.64</td>
</tr>
<tr>
<td>Kognitiv (BDI-II)</td>
<td>.23</td>
<td>.35</td>
<td>.44</td>
<td>.37</td>
<td>.64</td>
<td>.68</td>
</tr>
</tbody>
</table>

**Anmerkungen:** CDRS-R-Faktoren: beobachtete depressive Stimmung, Anhedonie, Gedanken an den Tod, körperliche Beschwerden, berichtete depressive Stimmung. BDI-II Faktoren: somatisch-affektiv, kognitiv.

### Tabelle 3a (oben)

**Korrelationskoeffizienten zwischen BDI-II (Items 1–11) und CDRS-R Items. Je intensiver der Grauton (0–.29; .30–.39; .40–.49; .50–.59; .60–.69), desto höher die Korrelation; Signifikanzgrenzen: r = .19, p = .05; r = .25, p = .01**

### Tabelle 3b (unten)

**Korrelationskoeffizienten zwischen BDI-II (Items 12–21) und CDRS-R Items. Je intensiver der Grauton (0–.29; .30–.39; .40–.49; .50–.59; .60–.69), desto höher die Korrelation; Signifikanzgrenzen: r = .19, p = .05; r = .25, p = .01**

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**Persönliches Autorenexemplar (e-Sonderdruck)**
sowohl in der CDRS-R ($M = 53.52; SD = 14.56$) einen signifikanten höheren Mittelwert auf als bei Jungen ($M = 46.43; SD = 10.87$), $t(103) = 2.35$, $p = .02$, als auch im BDI-II ($M = 26.64; SD = 11.56$) gegenüber den Jungen ($M = 19.61; SD = 11.36$), $t(103) = 2.77$, $p = .007$. Über alle depressiven Jugendlichen wurde ein hoher Zusammenhang zwischen dem Selbst- und Fremdbeurteilungsinstrument gefunden ($r = .67$, $p < .001$). Bei einer nach zeitlichem Abstand unterschiedlichen Auswertung zeigte sich, dass bei näher beieinander liegenden Erhebungszeitpunkten auch die Korrelation etwas höher ausfiel. Wurden CDRS-R und BDI-II am gleichen Tag erhoben ($N = 71$), zeigte sich eine Korrelation von $r = .73$. Diese unterschied sich allerdings nicht signifikant von der Korrelation, bei der die Messzeitpunkte bis zu einer Woche auseinander lagen ($z = -1.43$, $p = .15$).

Es zeigt sich, dass die inhaltlich ähnlichen Faktoren «soma

gleichbaren CDRS-R und BDI-II Items, so ergeben sich durchweg signifikante, zumeist mittlere Korrelationskoef-
fizienten ($p < .001$) (Tab. 4). Die höchste Korrelation zeigte sich zwischen dem CDRS-R und BDI-II Item zur Erfas-
sung von Selbstmordgedanken. In einigen Fällen korrelier-
ten CDRS-R Items höher mit inhaltlich weniger nahe lie-
genden BDI-II Items, wie zum Beispiel das CDRS-R Item «depressive Stimmung» welches am Höchsten mit dem BDI-II Item «Bestrafungsgefühl» korreliert. Von 11 inhit-
al gleichbaren CDRS-R und BDI-II Items korrelier-
ren acht tatsächlich auch am höchsten miteinander.

Bei näherer Betrachtung von Drittvariablen in ihrer Aus-

wirkung auf die Höhe der Zusammenhänge, fand sich bei
getrennter Auswertung nach Geschlecht bei weiblichen

Teilnehmern zwischen Selbst- und Fremdbeurteilungs-

instrument eine höhere, aber nicht signifikant höhere Korre-
lation ($r = .67$, $p < .001$) als bei männlichen Teilnehmern

($r = .60$, $p < .01$; $z = -.54$, $p = .59$). Weiterhin zeigten Pa-
tienten, die eine komorbide Störung aufwiesen, eine ge-
grere, aber nicht signifikant geringere Übereinstimmung
zwischen Selbst- und Klinikerurteil ($r = .58$, $p < .001$) als

Patienten ohne komorbide Störung ($r = .73$, $p < .001$; $z =
-1.29$, $p = .19$). Es konnten weiterhin keine Unterschiede

hinsichtlich der Übereinstimmung zwischen stationären ($r = .67$, $p < .01$) und ambulanten Patienten ($r = .68$, $p < .001$) gefunden werden ($z = .10$, $p = .92$). Jugendliche mit einem

IQ unter 100 zeigten eine niedrigere Übereinstimmung ($r$}
= .55, \( p < .001 \) als diejenigen mit einem IQ größer 100 (\( r = .67, p < .001 \)), auch hier erwies sich der Unterschied als nicht signifikant, \( z = -.86, p = .39 \).

Die Analyse der Diskrepanzwerte ergab zehn Unterschätzer (d. h. Jugendliche schätzen ihre Symptomatik im BDI-II relativ geringer ein als der Interviewer in der CDRS-R) und zehn Überschätzer (d. h. Jugendliche schätzen ihre Symptomatik im BDI-II relativ höher ein als der Interviewer in der CDRS-R; 85 Jugendliche waren konkordant. Eine Häufigkeitsauszählung mit den Variablen Geschlecht, ambulante vs. stationäre Behandlung und Komorbidität ergab in keiner der drei Variablen einen signifikanten Zusammenhang mit den drei Konkordanzkategorien. Auch eine Zusammenfassung der Unterschätzer und der Überschätzer in eine einzige Gruppe von Diskordanten ergab keine signifikante Beziehung zu den drei Variablen. Verzichtet man auf die (informationsreduzierende) Kategorisierung in Unter- und Überschätzer und verwendet die Diskrepanzwerte als quantitative Variable, ergibt sich weiterhin kein Unterschied bei Geschlecht und Komorbidität. In der Behandlungsform zeigt sich jedoch ein signifikanter Mittelwertunterschied, wonach die stationäre Behandlung eher in Richtung Unterschätzung tendieren (ambulante: \( M = 0.08; SD = 0.75 \); stationäre: \( M = -0.43; SD = 0.99 \)), \( t(103) = 2.43, p = .02 \). Außerdem bestehen Zusammenhänge zwischen Diskrepanzwert und Intelligenz sowie Alter. Die Korrelation zur Intelligenz beträgt \( r = .27; p = .01 \) (\( N = 89 \)), d. h. höhere Intelligenz ist mit relativer Überschätzung assoziiert. Zum Alter ergibt sich eine tendenziell signifikante Korrelation von \( r = -.18, (p = .06) \), d. h. ältere Jugendliche weisen eher eine Unterschätzung auf. Zur weiteren Analyse dieser Beziehungen wurden die Korrelationen zu den absoluten Diskrepanzwerten bestimmt (= absolute Abweichung von Null, was den Grad der Diskrepanz unabhängig von der Richtung widerspiegelt). Sowohl in der Korrelation zu Intelligenz wie auch zum Alter ergaben sich keine signifikanten Korrelationen \( (r = .00 \text{ bzw.} r = -.04) \), d. h. die Richtung spielt eine Rolle.

**Diskussion**

dem alle Items auf einem Generalfaktor laden und einzelne Items gleichzeitig noch spezifische Faktoren bilden können (vgl. Reise et al., 2010), wie es inzwischen auch für das BDI-II diskutiert wird (Brouwer, Meijer & Zevalkink 2013).


Literatur

gendpsychiatrischen Patienten. Psychotherapie, Psychosomatik, Medizinische Psychologie, 58, 63–68.


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Interessenkonflikte

– J. Straub hat keine Interessenkonflikte.


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Psychotherapeutic treatment of children and adolescents with depression. Review of the literature on cognitive-behavioral and interpersonal group therapies

6.5 Psychotherapeutic treatment of children and adolescents with depression. Review of the literature on cognitive-behavioral and interpersonal group therapies

Contribution of Joana Straub to the article:
J. Straub researched literature, wrote the manuscript, integrated remarks of the co-authors, revised the manuscript according to reviewer’s comments, and created tables.

Co-authors’ contributions to the article:
L. Nicolaus helped with literature research and creating tables. P.L. Plener, N. Sproeber, M.G. Koelch reviewed the draft and gave constructive remarks. They helped with revising the manuscript according to the reviewer’s comments.

Reference

Psychotherapeutische Behandlung von depressiven Kindern und Jugendlichen

Literaturübersicht zu kognitiv-behavioralen und interpersonellen Gruppentherapieverfahren


Hintergrund


Um das Suizidrisiko zu reduzieren, wurden interpersonelle Psychotherapien (KVT), eine interpersonelle Psychotherapie für Adoleszenz (IP A), das Medikament Fluoxetin oder eine Kombination aus KVT und Fluoxetin erhalten sollten. Hierbei ist zunächst der Psychotherapeut Vorrang zu gewähren.


Systematische Literaturübersicht

den u. Owen 1994; Maag u. Swearer 2001; Marzette 1997; Reinecke et al. 1998; Watanabe et al. 2007; Weisz et al. 2006) und die in diesen Reviews beschriebene Literatur, sofern nicht bereits durch die Literatursuche identifiziert, begutachtet.


In der vorliegenden Übersicht wurden nur Originalarbeiten unter Berücksichtigung der Parameter aufgenommen:

- Publikationen in einer Zeitschrift mit „Peer-review“-Verfahren (keine Dissertationen oder Buchbeiträge),
- Verwendung standardisierter Instrumente bzw. klinischer Interviews zur Erfassung von Depressionen,
- Vorliegen einer Depressionsdiagnose (ermittelt anhand der International Statistical Classification of Diseases...
Infobox 1

Elemente des Programms Coping with Depression Course for Adolescents
- Selbstbeobachtung
- Training sozialer Fertigkeiten
- Erhöhung angenehmer Aktivitäten
- Verringerung depressiver Gedanken
- Erlernen von Konfliktlösestrategien

Mögliche Varianten
- Elterntraining
- Auffrischungssitzungen

Infobox 2

Taking Action
- Psychoedukation
- Definition von Therapiezielen
- Erkennen des Fortschritts in Richtung Zielerreichung
- Training von „Coping“-Fertigkeiten
- Problemlösetraining
- Kognitive Umstrukturierung
- Aufbau eines positiven Selbstwerts

Infobox 3

Stimmungsprobleme bewältigen
- Psychoedukation
- Selbstbeobachtung
- Verhaltensaktivierung
- Entspannungstraining
- Soziales Kompetenztraining
- Kognitive Umstrukturierung
- Förderung der Problemlösefähigkeiten

Infobox 4

Manualized Intervention to Cope with Depressive Symptoms
- Psychoedukation
- Selbstbeobachtung
- Kognitive Umstrukturierung
- Förderung der Problemlösefähigkeiten
- Verhaltensaktivierung
- Umgang mit Krisen

and Related Health Problems (ICD), des Diagnostic and Statistical Manual of Mental Disorders (DSM) oder der erreichten „Cut-off“-Werte in relevanten Fragebogen oder Interviews].


Unter Berücksichtigung der oben genannten Kriterien konnten schlussendlich 25 Studien aufgenommen werden (Tab. 1, 2, 3). Davon bezogen sich jeweils 2 Studien auf die gleiche Stichprobe; deshalb werden sie in einer Zeile aufgeführt.

Ergebnisse

Die meisten Studien untersuchten die Wirksamkeit von kognitiv-behavioralen Gruppentherapieverfahren (Tab. 1). 2 Studien untersuchten die interpersonelle Therapie (Tab. 2) und 2 eine Mischung aus beiden Verfahren (Tab. 1, 2). Die Länge der Therapien varierte deutlich von einer 5-wöchigen Therapiedauer mit jeweils einer Sitzung/Woche á 90 min (Tab. 3) bis hin zu einer 16-wöchigen Therapiedauer mit jeweils einer Sitzung/Woche à 90–120 min (Tab. 2).

Es gab lediglich 3 Studien, die die Wirksamkeit von Depressionsgruppentherapien im deutschen Sprachraum untersuchten, wobei sich 2 davon auf dieselbe Stichprobe bezogen (Tab. 3). Sieben Studien fokussierten sich auf Kinder und 18 Studien auf Jugendliche und junge Erwachsene. Neun Programme wurden in Schulen, 14 im ambulanten Setting, eines im stationären Setting und eines online durchgeführt.


Gruppentherapieverfahren

Im folgenden Abschnitt werden die beiden gängigsten englischsprachigen kognitiv-verhaltenstherapeutischen Gruppentherapieverfahren, anschließend die interpersonelle Gruppentherapie für Jugendliche und die 2 deutschen kognitiv-verhaltenstherapeutischen Gruppentherapieverfahren skizziert.


In einer deutschen Metaanalyse wurden insgesamt 24 deutsch- und englischsprachige Studien, die „Coping with Depression“ (CWD) bei Jugendlichen und Erwachsenen im Einzel- und Gruppensetting untersuchten, mit dem Ergebnis einer hohen Effektstärke (ES =1,45) einbezogen. Die Behandlungseffekte blieben dabei mittelfristig stabil (Kühner 2003). In einer holländischen Metaanalyse wur-...
Zusammenfassung · Abstract

Psychotherapeutische Behandlung von depressiven Kindern und Jugendlichen. Literaturübersicht zu kognitiv-behavioralen und interpersonellen Gruppentherapieverfahren

Zusammenfassung

Hintergrund. Depression beschreibt eine psychische Störung mit stark beeinträchtigenden Symptomen (z. B. erhöhte Suizidalität), die auch im Kindes- und Jugendalter eine hohe Prävalenzrate aufweist und häufig einen chronischen Verlauf zeigt. Sowohl die kognitive Verhaltenstherapie (KVT) als auch die interpersonelle Therapie stellen derzeit nach diversen Leitlinien die Therapien der ersten Wahl dar.


Ergebnisse. Wirksamkeitsnachweise existieren v. a. für englischsprachige kognitiv-verhaltenstherapeutische Gruppentherapieprogramme (Effektstärken zwischen 0,02 und 1,34) und nur wenige für die interpersonelle Gruppentherapie. Für den deutschen Sprachraum liegen wenige Studien zu kognitiv-verhaltenstherapeutischen Gruppentherapien und gemäß dem Wissen der Autoren keine zur interpersonellen Gruppentherapie vor.


Schlüsselwörter
Wirkung der Behandlung · Datensammlung · Deutsch · Englisch · Depression

Psychotherapeutic treatment of children and adolescents with depression. Review of the literature on cognitive-behavioral and interpersonal group therapies

Abstract

Background. Depression is a psychiatric disorder with debilitating symptoms (e.g. suicidal behavior) even in children and adolescents, and the disorder shows a chronic course in many cases. According to psychiatric guidelines, cognitive behavioral therapy and interpersonal therapy are the psychotherapeutic methods of choice.

Aim. This article gives an overview of the current studies on cognitive behavioral and interpersonal group therapy programs for the treatment of depression in children and adolescents as well as a short illustration of the most prevalent therapy programs.

Material and methods. A literature research (PsychInfo, Psycdex, Pubmed) revealed 280 hits. After a review of all titles and abstracts 25 studies were included in this study.

Results. Efficacy studies mainly exist for cognitive behavioral group therapy programs (effect sizes ranged from 0.02 to 1.34) from English-speaking countries. There are only a few German programs available. With respect to interpersonal group therapy there are only a few articles published in English and to the best of our knowledge none in German.

Conclusion. There is a great need for further studies that investigate the efficacy of group therapies for the treatment of depression in children and adolescents especially in German-speaking countries.

Keywords
Treatment efficacy · Data collection · German · English · Depression


Joana Straub · Leonie Nicolaus · Paul L. Plener · Nina Spröber · Michael Köchler

Die Selbstkontrolltherapie „Taking Action“ (Stark et al. 2004; Stark et al. 1996) wurde eigentlich als Einzeltherapie konzipiert, kann aber auch in Gruppen angewendet werden. Sie umfasst 3 Behandlungsphasen mit jeweils 4 Sitzungen zu jeweils einer Stunde. In der ersten Phase werden gemeinsam von Patient und Therapeut 1 oder 2 Problembereiche definiert (z. B. Trauer; interpersonale Defizite), die Rolle des Patienten und die des Therapeuten geklärt und ein
<table>
<thead>
<tr>
<th>Studie</th>
<th>Therapieprogramm</th>
<th>Anzahl (n; Alter; Klasse)</th>
<th>Anzahl (n) der Sitzungen/Woche</th>
<th>Dauer je Sitzung</th>
<th>Setting</th>
<th>Abhängige Messinstrumente</th>
<th>Studiendesign</th>
<th>Resultate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clarke et al. (2013)</td>
<td>CWD-A</td>
<td>(13–18 J.)</td>
<td>2 Sitzungen/Woche</td>
<td>120 min/Sitzung</td>
<td>Ambulant</td>
<td>CES-D HAM-D K-SADS</td>
<td>RCT</td>
<td>IG: CWD-A + TAU KG: TAU</td>
</tr>
<tr>
<td>Gaynor u. Lawrence (2002)</td>
<td>CWD-A + interpersonelles Lernen (LIVE)</td>
<td>(14–18 J.)</td>
<td>2 Sitzungen/Woche</td>
<td>120 min/Sitzung</td>
<td>Ambulant</td>
<td>NIMH DISC HRSD BDI</td>
<td>RCT</td>
<td>IG1/IG2/IG3 &gt; KG</td>
</tr>
<tr>
<td>De Cuypers et al. (2004)</td>
<td>„Taking action“ + Einbezug der Eltern</td>
<td>(9–11 J.)</td>
<td>1 Sitzung/Woche</td>
<td>60 min/Sitzung</td>
<td>Ambulant</td>
<td>CDI SPRC STAC CBCL CAS</td>
<td>RCT</td>
<td>IG: Taking action KG: Warte</td>
</tr>
</tbody>
</table>
### Tab. 1: Kognitiv-verhaltenstherapeutische Gruppentherapieverfahren zur Behandlung von depressiven Kindern und Jugendlichen im englischsprachigen Raum (Fortsetzung)

<table>
<thead>
<tr>
<th>Studie</th>
<th>Therapieprogramm</th>
<th>Anzahl (n; Alter; Klasse)</th>
<th>Anzahl (n) der Sitzungen</th>
<th>Dauer je Sitzung</th>
<th>Weißlich (%)</th>
<th>Setting</th>
<th>Abhängige Messinstrumente</th>
<th>Studiendesign</th>
<th>Resultate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Van der Zanden et al. (2012)</td>
<td>KVT</td>
<td>244 (16–25 J.)</td>
<td>6 Wochen</td>
<td>1 Sitzung/Woche 90 min/Sitzung</td>
<td>84,4 Online-Gruppen-Kurs</td>
<td>CES-D HADS RCT IG: Online-Gruppen-KVT KG: Warteliste</td>
<td>IG &gt; KG d=0,94</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kowalenko et al. (2005)</td>
<td>KVT + IPT</td>
<td>82 (13–16 J.; 9. Klasse)</td>
<td>8 Wochen</td>
<td>1 Sitzung/Woche 90 min/Sitzung</td>
<td>100 Schule CDI ACS CATS IG: ACE KG: Warteliste</td>
<td>IG &gt; KG η²=0,078</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weisz et al. (1997)</td>
<td>PASCET</td>
<td>48 (M =9,6 J.; 3.–6. Klasse)</td>
<td>8 Sitzungen</td>
<td>50 min/Sitzung</td>
<td>45,83 Schule CDI CDRS-R IG: PASCET KG: Warteliste</td>
<td>IG &gt; KG d=0,48–0,52 (CDI) d=0,16–0,39 (CDRS-R) n.s.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reed (1994)</td>
<td>Strukturierte Lerntherapie (SLT, Veränderung dysfunktionaler Kognitionen)</td>
<td>18 (14–19 J.)</td>
<td>12 Wochen 2-wöchige Sitzungen</td>
<td>60 min/Sitzung</td>
<td>50 Ambulant CDI BDI DFE PIC MMPI IG: soziales Kompetenztraining KG: Warteliste</td>
<td>IG &gt; KG d=−0,66a (Nur wirksam bei männlichen Jugendlichen)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lerner u. Clum (1990)</td>
<td>Soziales Kompetenztraining vs. supportive Gruppentherapie</td>
<td>18 (18–24 J.)</td>
<td>5–7 Wochen 10 Sitzungen</td>
<td>90 min/Sitzung</td>
<td>78 Ambulant MSSI Modified MEPS PSI BDI HS UCLA Loneliness Scale IG1&gt;IG2 d=−0,55b</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Butler et al. (1980)</td>
<td>Rollenspiele vs. kognitive Umstrukturierung</td>
<td>56 (5.–6. Klasse)</td>
<td>10 Wochen 1 Sitzung/Woche</td>
<td>60 min/Sitzung</td>
<td>37,5 Schule CDI Self-Esteem Scale Moyal-Mieczisz Stimulus Appraisal Questionnaire IG: soziales Kompetenztraining KG: Placebo, Aufmerksamkeit KG2: Klassenzimmer</td>
<td>IG1&gt;IG2/KG1/KG2 IG1: d=0,28a IG2: d=0,09a</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ACS Adolescent Coping Scale, BDI Beck Depression Inventory, BID Bellevue Index of Depression, CAS Child Assessment Schedule, CBCL Child Behavior Checklist, CBQC Cognitive Bias Questionnaire for Children, CDI Child Depression Inventory, CDRS-R Children’s Depression Rating Scale-Revised, CDS Child Depression Scale, CES-D Center for Epidemiologic Studies-Depression Scale, CGAS Children’s Global Adjustment Scale, CWD Copying with Depression Course, CWD-A Copying with Depression Course for Adolescents, DISC National Institute of Mental Health Diagnostic Schedule for Children, Epidemiological Version/Present Version, GAF Global Assessment of Functioning Scale, HADS Hospital Anxiety and Depression Scale, HAM-D/HDRS Hamilton Depression Rating Scale, HS Hopelessness Scale, IPT interpersonelle Psychotherapie, J. Jahre, KG Kontrollgruppe, K-SADS-E/-P Schedule for Affective Disorders and Schizophrenia for School-Aged Children, KVT Kognitive Verhaltenstherapie, LOT Life-Orientation Test, MASC Multidimensional Anxiety Scale for Children, MMPI Minnesota Multiphasic Personality Inventory, Modified MEPS Modified Means-Ends Problem-Solving Procedure, MSSI Modified Scale for Suicidal Ideations, PASCET Primary and Secondary Control Enhancement Training, PIC Personality Inventory for Children, PMR progressive Muskelrelaxation, PSI Problem Solving Inventory, RADS Reynolds Adolescent Depression Scale, RCT randomisiertes kontrolliertes Design, SASCA Social Adjustment Scale for Children and Adolescents, SPCC Self-Perception Profile for Children, STAI State-Trait Anxiety Inventory for Children; *Erfolgsraten entnommen aus Weisz et al. (2006); †Erfolgsraten entnommen aus Reineke et al. (1998).
Tab. 2 Interpersonelle Gruppentherapieverfahren zur Behandlung von depressiven Jugendlichen im englischsprachigen Raum

<table>
<thead>
<tr>
<th>Studie</th>
<th>Therapieprogramm</th>
<th>Anzahl (n; Alter; Klasse)</th>
<th>Anzahl (n) der Sitzungen; Dauer je Sitzung</th>
<th>Weiblich (%)</th>
<th>Setting</th>
<th>Abhängige Messinstrumente</th>
<th>Studien-design</th>
<th>Resultate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rossello et al. (2008)</td>
<td>KVT IPT</td>
<td>112 (12–18 J.; 6–12 Klasse)</td>
<td>12 Wochen 1 Sitzung/ Woche 60 min/ Sitzung (Einzelsetting) 120 min/ Sitzung (Gruppensetting)</td>
<td>55,4</td>
<td>Ambulant</td>
<td>PHCSCS CBCL-A CBCL-P SASCA DISC</td>
<td>RCT IG1: KVT (Einzelsetting) IG2: KVT (Gruppen-setting) IG3: IPT (Einzelsetting) IG4: IPT (Gruppen-setting)</td>
<td>CBT &gt; IPT (unabhängig von Format) d=0,43 Einzelsetting = Gruppensetting d=0,18 n.s.</td>
</tr>
<tr>
<td>Miller et al. (2008)</td>
<td>IPT-PA</td>
<td>11 (14–18 J.)</td>
<td>12 Wochen 1 Sitzung/ Woche 75 min/ Sitzung</td>
<td>100</td>
<td>Schule</td>
<td>K-SADS BDI HRSD CGI</td>
<td>Pilotstudie</td>
<td>8 von 11 Jugendlichen erfüllten nicht Teilnahme nicht mehr die Kriterien einer Depression; signifikante (p&lt;0,05) Reduktion der Depressionswerte</td>
</tr>
<tr>
<td>Bolton et al. (2007)</td>
<td>IPT-G Spieltherapie</td>
<td>314 (14–17 J.)</td>
<td>16 Wochen 1 Sitzung/ Woche 90–120 min/ Sitzung</td>
<td>57</td>
<td>Schule</td>
<td>APAI RCT IG1: IPT-G IG2:Spieltherapie KG: Warteliste</td>
<td>IG1&gt; KG (nur Mädchen; „intention to treat“) p=0,02 IG2= KG</td>
<td></td>
</tr>
</tbody>
</table>


Patientenvertrag unterschrieben. In der zweiten Phase werden die Probleme analysiert, spezifische Interventionsformen ausgewählt und ein Behandlungsplan erstellt. Typische Inhalte der Sitzungen sind die Rolle in der Adoleszenz und individuelle oder interpersonelle Schwierigkeiten. Ziel ist es, dass die Jugendlichen lernen, aktive Kommunikationsstrategien zu entwickeln, ihre Gefühle auszudrücken und sich ein soziales Umfeld aufzubauen. In der dritten Phase wird der Patient auf das Ende der Therapie vorbereitet und darin geschult, auch mit zukünftigen Problemen adäquat umgehen zu können.


wurde. Außerdem befasst sich ein Schwerpunkt des Programms mit dem Umgang mit Krisen (z. B. Suizidgefährdung), selbstverletzendem Verhalten). Im Zuge dessen lernen die Teilnehmer zunächst ihren Gefühlszustand nach einem Ampelsystem (grün: ausgeglichene Stimmung; rot: kri-.

Diskussion

Ein Ergebnis der systematischen Literaturübersicht ist, dass evaluierte und publizier-


Determinanten der Wirksamkeit

mehrheitlichen zufriedenheit der Patienten weniger ausdrücklich Notwendige stattgefunden haben.

Insgesamt zeigte sich, dass in den meis-

ten Studien die Interventionsgruppe nach Behandlung signifikant geringere Depres-

sionsscores (CWD-A), mit allerdings sehr he-

terogenen Effektstärken. Besonders inter-

essant ist dabei, dass der Online-CWD-A eine verhältnismäßig hohe Effektstärke aufweist. Eine Begründung könnte sein, dass die Jugendlichen und jungen Erwachsenen, die sich für den Onlinekurs angemeldet haben, dies aus einer starken Eigenmotivation heraus getan haben und nicht fremd motiviert wurden, wie es im Fall ambulanter Therapien mit Kindern und Jugendlichen häufiger der Fall ist (Matteja 2008). Vielleicht führt auch die Anonymität des Chatrooms zu einer stärkeren Selbstöffnung, die wiederum den Therapieprozess erleichtert.


| Studie | Therapi- | Anzahl | Anzahl | Weich- | Setting | Ab- | Stu- | Resultate |
|--------|----------|--------|--------|--------|---------| hängige | dien- | |
| Ihle et al. (2003) | Stimmungsprobleme bewältigen | 21 | (16–25 J.) | 57,14 | 3 Gruppen | ambulant | 90 min | Pilotstudie |
| Ihle und Jahnke (ihle u. Jahnke 2003) | | | (54% Komorbiditäten) | | | | | | |
| Straub et al. (2013) | MICHI | 9 | (13–18 J.) | 55,56 | Statio- | CDRS-R | Pilot- | Prä-post Vergleich |
| | | | | | när | | studie | | |

Behandlung nicht erfasst worden seien. So kann es sich dabei auch um eine Intervention ähnlich einer Depressionseinzeltherapie gehandelt haben, was die vergleichbaren Effekte erklären würde. Die Autoren der zweiten Studie (Clarke et al. 2002) begründeten ihr Ergebnis damit, dass ihre Stichprobe (depressive Jugendliche mit mindestens einem depressiven Elternteil) von anderen depressiven Stichproben abweiche (betroffene Jugendliche sprechen schlechter auf Therapie an); dies erklären, warum die Ergebnisse der TAU-Gruppe nicht signifikant von der Interventionsgruppe abwichen.


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Einleitung therapeutischer Aspekte

Interessenkonflikte.

Literatur
Reed MK (1994) Social skills training to reduce depression in adolescents. Adolescence 29(114):293–302
Innovations in Practice: MICHI, a brief cognitive-behavioural group therapy for adolescents with depression - a pilot study of feasibility in an inpatient setting

6.6 Innovations in Practice: MICHI, a brief cognitive-behavioural group therapy for adolescents with depression - a pilot study of feasibility in an inpatient setting

Contribution of J. Straub to the article:
J. Straub coordinated the study procedure, recruited participants, assessed suicidal ideation and behaviour on a weekly basis, and scheduled diagnostic as well as psychotherapeutic appointments. She controlled the return of questionnaires and executed diagnostic assessments that didn’t have to be done by an independent evaluator (e.g. IQ measurements). She executed weekly group therapy sessions. She did data acquisition, data input, executed statistical analyses, and interpreted statistical outcomes. She researched literature, wrote the manuscript, integrated remarks of the co-authors, revised the manuscript according to reviewer’s comments, and created figures and tables.

Co-authors’ contributions to the article:
Gonzalez-Aracil, I. and Voit, A. made decisions on the experimental design and conceptualized the study under supervision. They held weekly group therapy sessions, configured diagnostic instruments, and, under supervision, developed a diagnostic instrument for the assessment of acceptance. They helped with data acquisition and generation of the data matrix. They reviewed the draft and gave constructive remarks. N. Sproeber and M.G. Koelch supervised decisions on the experimental design and conceptualized the study. They supervised the conduction of weekly group therapy sessions as well as the configuration of diagnostic instruments. They reviewed the draft and gave constructive remarks and helped with revising the manuscript according to the reviewer’s comments. P.L. Plener and J.M. Fegert reviewed the draft and gave constructive remarks.

Reference

Innovations in Practice: MICHI, a brief cognitive-behavioural group therapy for adolescents with depression – a pilot study of feasibility in an inpatient setting

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Background: Group therapy is an economic intervention, allowing for fast access, for the treatment of several depressed adolescents simultaneously; evaluated manualised programs, however, are scarce.

Method: Nine depressive adolescent inpatients (M = 16.33 years; SD = 1.92) participated between October 2009 and March 2010 in a brief manualised group therapy programme (MICHI), which was evaluated with respect to feasibility and trends of efficacy.

Results: MICHI demonstrated good feasibility, was positively evaluated by the participants by means of an evaluation questionnaire ranging from 1 (very bad) to 10 (very good) (M = 7.22; SD = 1.79), and showed significant reduction of depressive symptoms (z = −2.66, p = .008) assessed by means of a clinical interview.

Conclusions: Feasibility of MICHI was demonstrated and larger trials for efficacy will follow.

Key Practitioner Message:
- MICHI uniquely combines the factors of a cognitive-behavioural, brief and group psychotherapy, as all those factors on their own have been proven to be effective in the treatment of depression in adolescents
- MICHI was carried out with nine mildly to severely depressed inpatient adolescents and demonstrated good feasibility
- The pretest and posttest comparison demonstrated significant reduction in depression scores and reduced suicidal ideation
- Due to its brevity as well as the group format, MICHI allows fast access and treatment of several patients at the same time, reserving long-term treatment for patients who fail to respond

Keywords: Depression; adolescents; brief psychotherapy; cognitive-behavioural group intervention

Introduction

About 18% of adolescents have experienced symptoms of depression at least once in their lives. Untreated depression increases the risk for concomitant disorders, a chronic course of the disorder and numerous negative effects (Saluja et al., 2004). This fact highlights the need for timely intervention for depressed adolescents (Clarke et al., 2009). As cost efficacy is a worldwide issue in healthcare systems, and availability of individual therapy is often restricted for several reasons, new forms of interventions that are effective, fast and economical are needed.

Recent meta-analyses investigating behavioural psychotherapy (CBT) for the treatment of depression demonstrate a positive indication for efficacy (Weisz, McCarty, & Valeri, 2006). Considering the duration of therapy, Goodyer et al. (2007) showed that after participation in a brief psychosocial intervention in an individual setting (M = three sessions), 21% of the moderately to severely depressed adolescents improved. Furthermore, the results of an eight-session manualised training programme for groups of children with mild to moderate depressive symptoms demonstrate that childhood depressive symptoms can be significantly reduced, with CDRS-R (Children’s Depression Rating Scale-Revised) (Poznanski & Mokros, 1996) scores declining three times more in the treatment group (12 points) than in the control group (Weisz, Thurber, Sweeney, Profitt, & LeGagnoux, 1997). Considering the therapy setting, results of a meta-analysis reported a mean effect size of 0.38 for group CBT (GCBT) and 0.37 for individual treatment, demonstrating no significant differences between the therapy settings (Weisz et al., 2006).

To our knowledge, there is no study investigating an intervention that combines all those factors and that might result in a brief GCBT for the treatment of mildly
to severely depressed adolescents; one that also lends itself to standardisation in the form of a manual and could be delivered to a large number of participants with a minimal amount of time and staff, and which would therefore offer an ideal option for research and treatment of depression (Oei & Dingle, 2008). The aim of our study was to examine the feasibility of the brief (four-session) GCBT ‘Manualised Intervention to Cope with depressive symptoms, Help strengthen resources, and Improve emotion regulation’ (MICHI, Japanese for ‘the way’) for mildly to severely depressed adolescents. Suicidality was assessed in this pilot study as well as first trends in efficacy with respect to reduction in depressive symptoms.

Method

Procedure
In Germany, there are prevention group programs for adolescents with depression, but so far no evaluated brief (four sessions) cognitive-behavioural group therapy programs for mildly to severely depressed adolescents. Therefore, little is known about group processes that might occur when working with depressed adolescents. According to the treatment of adolescent suicide attempters study (TASA), about half of the suicidal events occurred within the first four weeks of treatment (Brent et al., 2009). Furthermore, suicidality has a contagious effect, particularly among adolescents (Gould, Wallenstein, Kleinman, O’Carroll, & Mercy, 1990), possibly leading to a heightened risk within groups (e.g. by talking with each other about suicidal ideations). Because of the low psychosocial functioning of depressed adolescents, that could make attendance at regular therapy difficult, participation can be better guaranteed in an inpatient setting. With respect to those aspects, the aim to give patients the best support possible, and for ethical reasons, feasibility of MICHI was evaluated at first in a protected inpatient setting, between October 2009 and March 2010.

To qualify for inclusion in the study, participants were required to satisfy all the following criteria: aged between 13 and 18 years, an IQ ≥ 85, a raw-summary score ≥ 36 in the CDRS-R and a diagnosis of a mild, moderate or severe major depressive episode. Most comorbid diagnoses and antidepressant medications were allowed, as long as the diagnosis of a major depression was prevailing and medication had been stabilised for at least three weeks prior to the start. Participants with the diagnosis of bipolar disorder, schizophrenia and substance abuse had to be excluded from the study as those disorders render a different form of prevailing treatment. Further exclusion criteria are the initiation of drug treatment or psychotherapy while participating in MICHI.

The training programme was finally applied in two consecutive groups with weekly sessions lasting seven weeks in total (including the diagnostic process). The study was approved by the IRB of the University of Ulm. Participants were informed about the goals and course of therapy, the voluntary nature of their participation and confidentiality with regard to their data. Informed consent documents had to be signed by participants and their parents.

Intervention
Each session takes 90 min and includes in-session activities and reviews of the weekly homework. The sessions are built on a selection of methods used in clinical work and proven to be successful in the treatment of depression in youths. On the basis of the review of Bachmann, Bachmann, Rief, and Mattejat (2008), effective content for the treatment of depression in minors such as ‘psycho education’, ‘activities to feel more comfortable’, ‘challenging negative thinking’, ‘relaxation techniques’, ‘problem-solving’ and ‘involving parents and friends’ were included. Besides that, an ‘emergency plan for acute crisis’ was added.

The therapists were trained psychologists with a Master’s degree, each with prior GCBT experience with adolescents. They were initially trained and supervised weekly during the intervention by a fully licensed psychotherapist. Sessions were videotaped for supervision.

Participants
The sample consists of nine depressed adolescents (M = 16.43 years; five girls) who had been referred for inpatient treatment due to primary diagnoses of major depressive disorder (MDD). Four of them received outpatient psychiatric treatment before hospitalisation. Four participants fulfilled criteria for comorbid disorders, which were assessed by means of a standardised interview. Five were treated with antidepressants (see Table 1).

Measures
Feasibility was assessed through the participants’ attendance in the training and the training evaluation of the trainers (open question). The acceptance of the training programme and the evaluation of the contents of MICHI by the participants was accomplished by means of a process evaluation questionnaire, ranging from 1 (not true) to 5 (true) (mean values ≥ 3.5 indicate positive evaluation; mean values ≤ 2.5 indicate negative evaluation) as well as one global question assessing the evaluation of the whole training programme, ranging from 1 (very bad) to 10 (very good) (Likert scale). To assess the criteria for MDD as well as the improvement of depression, participants were interviewed by a clinical psychologist using the CDRS-R before and after participation in MICHI. The CDRS-R is a semi-structured, clinician-rated interview inquiring about symptoms of depression in children and adolescents. Suicidal ideation was assessed by means of item 13 of the CDRS-R. Pre- and posttest differences were analysed by means of the Wilcoxon signed-rank test (PASW statistics 18).

Results

Feasibility of MICHI
Four of nine adolescents participated in each session, with four participants missing one session and one participant missing two sessions, demonstrating fair attendance overall. Both trainers evaluated the manual as well-structured, that a lead time of about 30 min per session was sufficient and that it was fun to conduct MICHI. They also made proposals for the improvement of

Table 1. Demographics of the inpatients

<table>
<thead>
<tr>
<th>Age</th>
<th>IQ</th>
<th>Main diagnosis</th>
<th>Comorbid disorders</th>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>M = 16.43 years</td>
<td>M = 99.75</td>
<td>F32.0 Mild depressive episode (N = 1)</td>
<td>F42 Obsessive-compulsive disorder (N = 1)</td>
<td>Antidepressants (N = 5)</td>
</tr>
<tr>
<td>SD = 1.68 [13; 00–18; 06]</td>
<td>SD = 10.06 [87–116]</td>
<td>F32.1 Moderate depressive episode (N = 5)</td>
<td>F40.1 Social phobia (N = 1)</td>
<td>First generation antipsychotics (N = 2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>F32.2 Severe depressive episode (N = 2)</td>
<td>F90.1 Hyperkinetic conduct disorder (N = 1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>F33.1 Recurrent depressive episode (N = 1)</td>
<td>F43.1 Posttraumatic stress disorder (N = 1)</td>
<td></td>
</tr>
</tbody>
</table>

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the manual and stated that the second session was too overloaded and that 90 min per session is too long to guarantee concentrated participation. The global evaluation revealed that adolescents rated the training programme as positive and effective overall (M = 7.22; SD = 1.79). The results of the evaluation questionnaire are demonstrated in Table 2.

Of the contents applied in MICHI, participants rated development of an ‘emergency plan for acute crisis’ (M = 3.6) as helpful and positive, and ‘relaxation techniques’ (M = 2.1) as less helpful. All other elements were rated rather neutrally.

**Efficacy of MICHI**

A positive trend, with regard to the reduction in depression symptoms before and after participation in MICHI, was indicated by comparison of the CDRS-R pretest (M = 56.22; SD = 9.28) and posttest (M = 48.11; SD = 8.34), which demonstrated positive efficacy (z = −2.66, p = .008). With regard to suicidality, six of nine patients demonstrated none to mild and three patients demonstrated moderate to severe suicidal ideation before participation in MICHI. At the end of the programme, eight of nine patients demonstrated none to mild and only one patient demonstrated moderate to severe suicidal ideation. Therefore, we observed a reduction in suicidality in the pretest and posttest comparison.

**Discussion**

The aim of this pilot study was the evaluation of feasibility of a newly developed, brief, manualised cognitive-behavioural group therapy for the treatment of depression in adolescents. Considering feasibility, the attendance of the participants was fair and could be improved by the establishment of a reinforcement system in future applications. In response to feedback from the trainers, sessions will be shortened to 60–75 min each and the contents of session two will be reorganised, resulting in five regular sessions. Furthermore, adolescents evaluated the whole training programme positively. However, they doubted that the things learnt would help them with their family life or leisure time. This needs to be interpreted with an eye on the inpatient setting, which itself hampers transfer to daily life.

The content of ‘relaxation techniques’ was evaluated as less helpful, a finding supported by Petermann (2010), who recently stated that an acute depressive episode is a contraindication for relaxation techniques. Furthermore, participants rated the unique element ‘emergency plan for acute crisis’ as very helpful, demonstrating the need for concrete steps about how to behave should a crisis arise.

Regarding the efficacy of MICHI, CDRS-R scores declined significantly with a total drop of 8.11 points, slightly less than the reduction found by Weisz et al. (1997), still delivering promising results for further investigation. Furthermore, suicidal ideation was reduced after participation in MICHI, which allows the execution of MICHI in an ambulant setting as long as the trainers are experienced in the clarification and handling of suicidal ideations. Due to the contagious effect of suicidality, it is very important that clients are not allowed to discuss suicidal thoughts or past behaviour within the group or outside the sessions, but they can talk with the therapists individually.

Findings with regard to efficacy have several limitations. First, the number of participants is very small. Second, six of nine patients received medication. We tried to overcome that by including only patients whose medication was stabilised three weeks prior to the start, but who still demonstrated symptoms of depression. Third, the inpatient setting can influence the results. Fourth, the absence of a control group or follow-up assessment allows only weak conclusions about efficacy and none about long-term effects. Therefore, in this study, we can only speak of trends in efficacy but in a follow-up study, MICHI will be investigated with a larger sample in a controlled outpatient setting, and using a longitudinal design.

As cognitive behaviour therapy is normally an expensive intervention, taking up to 16 sessions, our following results indicate a strong case for using a brief cognitive-behavioural intervention as the first line of treatment, and reserving long-term CBT for those patients who fail to respond (Harrington, Whittaker, Shoebridge, & Campbell, 1998).

**Acknowledgements**

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All authors have declared that they have no competing or potential conflicts of interest.

**References**


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**Table 2. Evaluation of MICHI (mean values ≥ 3.5 indicate positive evaluation; mean values ≤ 2.5 indicate negative evaluation)**

<table>
<thead>
<tr>
<th>Items of the process evaluation questionnaire</th>
<th>Mean value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Structure of the training programme</td>
<td>4</td>
</tr>
<tr>
<td>Comprehensibility of the contents</td>
<td>4.22</td>
</tr>
<tr>
<td>Importance of the contents</td>
<td>4.11</td>
</tr>
<tr>
<td>Feeling comfortable in learning with others</td>
<td>3.78</td>
</tr>
<tr>
<td>Feeling comfortable within the group</td>
<td>3.56</td>
</tr>
<tr>
<td>Feeling comfortable with the trainers</td>
<td>4.11</td>
</tr>
<tr>
<td>Feeling well understood by the trainers</td>
<td>4.11</td>
</tr>
<tr>
<td>Estimation that MICHI could help other depressed adolescents, too</td>
<td>3.56</td>
</tr>
<tr>
<td>Estimation that MICHI would help them to manage their problems</td>
<td>1.89</td>
</tr>
<tr>
<td>Estimation that the things learned in MICHI would help them within their family life</td>
<td>2.22</td>
</tr>
<tr>
<td>Estimation that the things learned in MICHI would help them within their leisure time</td>
<td>2.11</td>
</tr>
</tbody>
</table>

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A brief cognitive-behavioural group therapy programme for the treatment of depression in adolescent outpatients: a pilot study

6.7 A brief cognitive-behavioural group therapy programme for the treatment of depression in adolescent outpatients: a pilot study

Contribution of J. Straub to the article:
J. Straub coordinated the study procedure and recruited participants. She executed weekly group therapy sessions, assessed suicidal ideation and behaviour on a weekly basis, and scheduled diagnostic as well as psychotherapeutic appointments. She controlled the return of questionnaires and executed diagnostic assessments that didn’t have to be done by an independent evaluator (e.g. IQ measurements). She did data acquisition, generated the data matrix, did data input, executed statistical analyses, and interpreted statistical outcomes. She researched literature, wrote the manuscript, integrated remarks of the co-authors, revised the manuscript according to reviewer’s comments, and created figures and tables.

Co-authors’ contributions to the article:
M. Bonenberger was co-therapist in weekly group therapy sessions, helped with data acquisition, reviewed the draft and gave constructive remarks. N. Sproeber and M.G. Koelch supervised decisions on the experimental design and conceptualized and coordinated the study. They supervised the conduction of weekly group therapy sessions. They reviewed the draft and gave constructive remarks and helped with revising the manuscript according to the reviewer’s comments. P.L. Plener and J.M. Fegert reviewed the draft and gave constructive remarks.

Reference
A brief cognitive-behavioural group therapy programme for the treatment of depression in adolescent outpatients: a pilot study

Joana Straub1*, Nina Sproeber1, Paul L Plener1, Joerg M Fegert1, Martina Bonenberger1 and Michael G Koelch1,2

Abstract

Background: The goal of this pilot study was to examine the feasibility and clinical outcomes of a brief (6-session) group therapy programme in adolescent outpatients with depression. The programme had previously been assessed in in-patients, with positive results.

Methods: A total of 15 outpatients aged 13 to 18 years took part in the programme between October 2010 and May 2011, in 3 separate groups of 4–6 participants each. The outcomes measured were feasibility of the programme, as assessed by attendance rate, user feedback, fidelity of implementation, and response to treatment, as assessed by pre- and post-intervention measurement of depressive symptoms, quality of life, and suicidal ideation.

Results: The programme demonstrated good feasibility, with a mean attendance rate of 5.33 out of 6 sessions, a mean rating by participants on overall satisfaction with the programme of 7.21 out of 10 (SD = 1.89), and a 93% concurrence between the contents of the sessions and the contents of the treatment manual. Compared to baseline scores, depressive symptoms at follow-up test were significantly reduced, as assessed by the Children’s Depression Rating Scale Revised (F(1, 12) = 11.76, p < .01) and the Beck Depression Inventory Revision (F(1, 32) = 11.19, p < .01); quality of life improved, as assessed by the Inventory of Quality of Life (F(1, 31) = 5.27, p < .05); and suicidal ideation was reduced. No significant changes were seen on the measures of the Parent Rating Scale for Depression and the Clinical Global Impression scale.

Conclusions: Based on the results of this pilot study, it is feasible to further assess this brief outpatient treatment programme in a randomized controlled trial without further modifications.

Background

The rate of depressive disorders in German adolescents aged 11–17 years is reported to be 4.7% for males and 9.7% for females [1]. Up to two-thirds of depressed adolescents suffer from co-morbid disorders [2], and depression is often associated with poor health behaviours and social challenges as well as with an elevated risk for suicide [3]. Suicide is the second most common cause of death for adolescents in Europe [4]. Given the nature and associated risks of depression, the Global Burden of Disease Study of the World Health Organization [5] has identified it as one of the most prevalent and debilitating disorders worldwide.

Several authors have looked at factors that might affect the effectiveness of therapies for children and adolescents with depression. In a meta-analysis of cognitive behavioural therapy (CBT) treatments, Weisz et al. [6] found a mean effect size (comparable to Cohen’s d) of .34. Group therapy was found to have several advantages over individual therapy, as follows: the group process can positively affect recovery, group members can learn from each other and give each other feedback, there is less stigmatisation, and the process may be more economical. A disadvantage, however, is that individuals with social anxiety or introversion may not receive as much attention as other participants [7]. In a recent meta-regression analysis looking at treatments...
for depression in adults, Cuijpers et al. [8] found that more sessions per week led to a larger effect size while every additional week of therapy reduced the effect size, which suggests there may be advantages to interventions that are short and intensive. Goodyer et al. [9] found that about one-fifth of depressed adolescents responded to a brief initial intervention (mean of 3 sessions). Brief therapies have the advantage that they allow for faster access to treatment and can be offered as a first-line treatment, reserving longer therapies for individuals who fail to respond.

There are currently six cognitive behavioural therapy programmes available in Germany to depressed adolescents: three for the prevention of depression and three for treatment [10-15]. Of the treatment programmes, one is the German version of the Adolescent Coping With Depression Course (CWD-A), which consists of ten 2-hour sessions [12]; one provides individual treatment sessions [11]; and one is primarily for the treatment of performance problems that may affect symptoms of depression [14]. However, none of these options combines the potential advantages described above of an intervention that uses CBT, is brief, and is delivered via group therapy. This article describes a brief (6-session) manualised programme that was developed to fill this gap. The programme is titled “Manualised Intervention to Cope with depressive symptoms, Help strengthen resources, and Improve emotion regulation”, or MICHI, which is Japanese for “The Way” [16].

For safety reasons, as depression increases the risk for suicidal behaviour, the MICHI programme was first evaluated in in-patients [17]. The results of that initial pilot study, which was conducted in 9 adolescents (mean age = 16.33 years), showed good compliance in terms of the mean number of sessions attended (4.33 out of 5), positive user feedback on the programme content and the group leaders, improvement in symptoms of depression (CDRS-R: \[ z = -2.66; \ p = .008 \]) and reduction of suicidal ideation. Based on participants’ feedback, we changed several aspects of the programme, including reordering of the therapeutic contents, deleting some content such as relaxation techniques, and adding an extra session.

**Objectives of the pilot study**

Before evaluating MICHI in a randomized controlled trial, we chose to conduct a second pilot study, this time in out-patients. Overall reasons for conducting pilot studies are to test the feasibility of a process, and to obtain preliminary data on the response to treatment [18]. Feasibility was here defined through three measures. The first was attendance, since as depression goes hand in hand with a lowered level of psychosocial functioning, participants might be expected to miss some sessions. A participation rate of five out of six sessions (79%) was defined as acceptable [19]. The second measure was user acceptance, for which we designed a questionnaire that asked participants how favourably they viewed various elements of the programme. The third feasibility measure was fidelity of implementation; i.e., how closely the psychologists who conducted the sessions were adhering to the treatment protocol defined in the MICHI treatment manual. Fidelity rates for manualised treatments typically range between 80% and 94% [20-23], so we defined anything within this range as being acceptable. With respect to response to treatment, efficacy was assessed by administering diagnostic tests of depression pre- post-intervention and follow-up and looking to see if scores were reduced following treatment. Safety was assessed through pre- post-intervention and follow-up measurement of suicidal ideation, which is a frequent symptom of depression. Since one of the goals of MICHI is to educate patients on how to deal with acute crises and prevent suicidal behaviour, we hypothesized that suicidal ideation would be reduced after participation.

**Methods**

**Population**

The pilot study was carried out in 3 separate groups of 4 to 6 participants each, with the first group starting in October 2010, the second in February 2011, and the third in March 2011. Recruitment was done by asking clinicians of local outpatient child and adolescent psychiatry and other local outpatient mental health institutions to refer any suitable patients to attend an information meeting held by the MICHI group leaders. Individuals who expressed interest following this meeting were scheduled for a screening visit, and those found eligible were enrolled in the next available group. Participants had to be aged between 13 and 18 years and to have an IQ of at least 80, a raw summary score on the Children’s Depression Rating Scale Revised (CDRS-R) [24] of at least 36 [25], and a diagnosis of a mild, moderate, or severe major depressive episode according to ICD-10 criteria [26]. In order for the sample to be representative of a naturalistic population, it was decided to not exclude difficult-to-treat patients [27]. Thus, co-morbid diagnoses were permitted as long as symptoms of depression were the main cause of the patient seeking medical support; and antidepressant medication was permitted provided it was stable for at least 5 weeks prior to study start and during the study. Individuals with a diagnosis of bipolar disorder, schizophrenia, or severe substance abuse were excluded, as these disorders require a different form of treatment and could be disruptive to the group process. Finally, participants and their parents/guardians had to agree to not to initiate any new drug treatment or new form of psychotherapy while participating in MICHI.
The study was approved by the IRB of the University of Ulm, Germany, and informed consent was provided by participants and their parents or guardians.

Study design
As described in its treatment manual [16], MICHI is a CBT treatment that combines a number of therapeutic components widely acknowledged to represent the standard of care [28, 29]. All sessions included (1) psycho-education, (2) cognitive restructuring with the aim of reducing rumination [30], (3) behavioural activation, (4) resource activation, (5) enhancement of self-esteem, (6) problem-solving skills, (7) emotion regulation, (8) management of acute crises, and (9) prevention of relapse.

The programme included 5 weekly visits of 75 to 90 minutes in length, plus a “booster” session held 5.5 weeks after the last regular visit. An overview of the content and activities of the sessions is shown in Table 1. Each session included a review of what had been covered the previous week, provision of new information, therapist-assisted practice, homework for the coming week, assessment of mood using the Beck Depression Inventory–Revision (BDI-II) questionnaire [31], and the opportunity to talk to the therapist individually after the session in cases of acute crisis. Item 9 of the BDI-II, which asks about suicidal behaviour, was checked at every session, and if a participant reported current suicidal ideation, the programme supervisor was to be consulted in order to conduct a risk assessment and to decide if hospitalization was necessary. For Session 5, each participant was asked to bring along a “person of trust”, either a family member or a friend, who would attend the session and be trained on how to support the patient to help prevent relapse as well as on step-wise problem solving.

The sessions were conducted according to the detailed instructions provided in the MICHI treatment manual, and were led by two of the manual’s co-authors (JS and MB) who are psychologists with master’s degrees and prior group CBT experience with adolescents. Both leaders were equally involved, and had predefined tasks to ensure that the same intervention was provided at all three MICHI groups. The group leaders were supervised by the manual’s main author and licensed psychotherapist (NS).

The study design is presented in Figure 1. Assessments were carried out prior to Session 1 (pre-intervention), following Session 5 (post-intervention), and between 1 and 2.5 weeks after the booster session (follow-up). Each of the 3 assessment periods spanned 10 days, to allow for evaluation of all participants in the group.

Diagnostic instruments
Screening measures included administration of the Kiddie Schedule for Affective Disorders and Schizophrenia, Present and Lifetime Version (K-SADS-PL) [32] to assess psychiatric disorders, and one of the following tests to assess intelligence: either the Wechsler Intelligence Scale for Children–Fourth Edition (WISC IV) [33], the Wechsler Adult Intelligence Scale (WAIS) [34], or the testing system for educational counselling (PSB) [35].

The primary outcomes for assessment of MICHI were: 1) feasibility of the programme, as assessed by attendance rate, user acceptance, and fidelity of implementation, and 2) preliminary data on the response to treatment assessed by the change in depressive symptoms, as measured by the CDRS-R total score. Attendance was defined as the percentage of sessions for which participants showed up. User acceptance was determined by having participants anonymously complete an ad hoc evaluation form containing 21 statements ($\alpha = .92$ in the present sample) that were rated on a scale of 1 (not true) to 5 (true) plus one global question regarding overall satisfaction with the programme, rated on a scale of 1 (very poor) to 10 (very good). To determine fidelity of implementation, all sessions were videotaped, and 25% were randomly selected and viewed by an independent clinician to see if the required elements in the MICHI treatment manual were being implemented. A 57-item checklist was employed in the rating, with each item scored as either present or absent. The CDRS-R is a semi-structured clinician-rated interview, consisting of 17 questions, which asks about symptoms of depression over the last 2 weeks [24]. A score of 36 or greater indicates evidence of clinically relevant symptoms of depression [25]. The interview has shown a high internal consistency in previous studies with larger sample sizes ($\alpha = .90$) [36] and $\alpha = .79$ in the present sample. The German version of the CDRS-R was used in this study [37]. The independent evaluators who performed the interview were blinded to the time points of measurement.

The secondary outcomes were changes in depression as measured by other instruments, changes in suicidal ideation, and changes in other measures of mental health. Two instruments were used for assessing depression over the last 2 weeks, one administered to the patient and the other to the parent/guardian: the BDI-II [31], which consists of 21 items ($\alpha = .95$ in the present sample), and the Parent Rating Scale for Depression (FBB-DES), which is part of the diagnostic system for mental disorders in childhood and adolescence (DIS-IVYPS-II) [38] and is based on the international classification systems ICD-10 and DSM-IV (29 items; $\alpha = .89$ in the present sample). Suicidal ideation was assessed by Item 13 of the CDRS-R (asking for suicidal ideations and suicide attempts). The question is answered using a 7-item scale ranging from “none to mild” (never thought about suicide or thought about it very seldom) to “moderate to severe” (thought about or attempted suicide within the last month). Other instruments used were the
### Table 1 Contents of MICHI sessions

<table>
<thead>
<tr>
<th>Session number</th>
<th>Contents</th>
<th>Exercises</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Session 1</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Get to know each other</td>
<td>• Postcards with different emotional motifs were displayed, and participants were encouraged to choose one that represented their depression best</td>
</tr>
<tr>
<td></td>
<td>• Psychoeducation about symptoms of depression</td>
<td>• Related to the postcards, each participant was asked to tell his/her symptoms, and group leaders highlighted typical symptoms of depression</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Homework: participants were asked to</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Think about individual possible causes for their depressive symptoms</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Conduct a positive activity each day and to evaluate how it affects their mood</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Bring an object to the next session that represents something they are good at/pride of (e.g., football)</td>
</tr>
<tr>
<td><strong>Session 2</strong></td>
<td>• Resource activation</td>
<td>• Participants showed the object they brought that represented something they were good at/pride of</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Participants were asked to name additional strengths and resources</td>
</tr>
<tr>
<td></td>
<td>• Input about relationship between thoughts, behaviour, and feelings</td>
<td>• Psychoeducation about causation of depression (e.g., neurotransmitters, genetics, stressors)</td>
</tr>
<tr>
<td></td>
<td>• Psychoeducation about aet causations of depression</td>
<td>• Homework: participants were asked to</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Focus on a positive and negative moment each day and to note down their behaviour, thoughts, and feelings in each moment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Note down compliments they receive or positive moments that happen to them in a diary</td>
</tr>
<tr>
<td><strong>Session 3</strong></td>
<td>• Enhancement of self-esteem</td>
<td>• Participants threw each other a ball, and each time they caught the ball they were asked to name a certain individual strength</td>
</tr>
<tr>
<td></td>
<td>• Increase of behavioural activation</td>
<td>• Participants were invited to write each other compliments in their diaries</td>
</tr>
<tr>
<td></td>
<td>• Psychoeducation about dysfunctional cognitions</td>
<td>• Input about the importance of positive self-esteem</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Input about how errors in reasoning, e.g., dichotomous thinking, negatively influences how one feels</td>
</tr>
<tr>
<td><strong>Session 4</strong></td>
<td>• Repetition of contents</td>
<td>• Participants listened to an audiotaped interview with a depressed girl who talked about her symptoms, and were asked to give her advice about what she could do to feel better, taking into account what they learned in MICHI so far</td>
</tr>
<tr>
<td></td>
<td>• Management of acute crises</td>
<td>• Discussion and input about how to behave in case of crises (e.g., suicidal ideation)</td>
</tr>
<tr>
<td></td>
<td>• Emotion regulation</td>
<td>• Identification of helpful skills</td>
</tr>
<tr>
<td></td>
<td>• Restructuring of dysfunctional cognitions</td>
<td>• Input about how to recognize negative thoughts and how to turn them into positive ones</td>
</tr>
<tr>
<td><strong>Session 5</strong></td>
<td>• Problem-solving skills prevention of relapse</td>
<td>• Participants learned how to solve problems in a theoretical stepwise manner; afterwards, they watched a video about a girl who is being bullied, and were asked how they would solve a problem like the one of the protagonist, taking into account the stepwise manner of problem-solving they learned before</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Participants brought a person of trust</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Conversation about how persons of trust can support participants in the future to prevent relapse</td>
</tr>
<tr>
<td><strong>Booster session 6</strong></td>
<td>• Recapitulation of contents of MICHI</td>
<td>• Contents of MICHI were repeated by means of a quiz</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Each participant was asked to recapitulate his/her mood since the last session of MICHI</td>
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<td></td>
<td>• In case they found themselves in a depressed mood, they were asked whether they were able to apply elements of MICHI to prevent themselves from relapse</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Participants were given a written case report of a depressed boy and were asked to advise him what he could do to feel better with reference to the contents learned in MICHI</td>
</tr>
</tbody>
</table>

Inventory for the Assessment of Quality of Life in Children and Adolescents (IQLC) [39], which consists of 7 items (α = .59 in the present sample) and assesses quality of life in the past week; the Clinical Global Impression (CGI) [40], which consists of 1 item and assesses severity of symptoms over the past week; and the Health of the Nation Outcome Scales for Children and Adolescents (HoNOSCA) [41], which consists of 13 items (α = .74 in
the present sample) and assesses psychosocial strain over the past month. The time points at which each instrument was administered are shown in Figure 1.

Statistical methods
All analyses were conducted using mixed effects repeated measures analysis (multi-level) for longitudinal data with an autoregressive covariance structure (AR1) and maximum likelihood estimation which is a contemporary method for handling missing data [42]. Comparisons between small samples were done by means of the Mann–Whitney test. Statistical analyses were performed using PASW statistics 18. For testing hypotheses, the significance level was set a priori at a two-tailed type I error rate of .05. Comparisons between small samples were done by means of the Mann–Whitney test. Statistical analyses were performed using PASW statistics 18. For testing hypotheses, the significance level was set a priori at a two-tailed type I error rate of .05.

Results
Patient disposition and characteristics
Patient disposition is shown in Figure 2. Of 22 adolescent outpatients who were referred for screening, 3 were screening failures (reasons: IQ < 80, CDRS-R score < 36, and patient started medication during the diagnostic period), and 4 declined to participate; 3 by their own choice and 1 where permission was refused by the mother. The pre-intervention CDRS-R scores of the 4 individuals who declined participation did not differ from those of the completers ($U = 14.5, z = -.51, p = .61$); however, 2 of these individuals differed from the others with respect to co-morbid diagnosis (social phobia). After MICHI, nine patients had further regular visits to a psychiatric clinic or practice, meeting with a psychiatrist/psychologist for approximately 30 minutes once every 1–3 months. These appointments helped to stabilize or support them. Two were referred for further weekly psychotherapy.

Demographic and diagnostic data of the patients who took part in the study are provided in Table 2. Mean age was 16.42 (SD = 1.43) years (range: 13.1 to 17.9 years), and 11 (73.3%) were female. Four (26.6%) had previously received psychological treatment, but none were receiving it currently or had received it within the last 12 months.
Programme feasibility
Nine (60%) participants attended all 6 sessions, 3 (20%) attended 5 sessions, 2 (13.3%) attended 4 sessions, and 1 (6.6%) attended 3 sessions. The overall attendance rate was 78.8%, with a mean of 5.33 out of 6 sessions attended. At Session 5, 11 participants (73.3%) brought a supportive person as requested, 2 (13.3%) came alone, and 2 (13.3%) did not show up. Of those who brought somebody, 5 came with their best friend, 3 with their mother, 2 with a sibling, and 1 with a social worker who worked with her family.

The results of the user feedback questionnaire are presented in Table 3. The mean ratings ranged from 2.29 to 4.14 out of 5. The highest ratings (≥4.0) were seen for the statements regarding whether participants liked being in the group with other adolescents, whether they felt the programme would be helpful for others, and whether they felt comfortable with and understood by the group leaders. The lowest ratings (<3.0) were seen for the statements regarding whether participants felt that what they had learned in the programme could be successfully applied to their daily life, family life, leisure time, and school; whether they felt that family members and friends could help them with problems in future; and whether the inclusion of family and friends had been helpful. The mean score for the global question on
overall satisfaction with the program was 7.21 (SD = 1.89) out of 10.

With respect to fidelity to the MICHI treatment manual, based on the findings of the independent clinician who rated videotapes of randomly selected sessions, there was a 93% concurrence between the manualised treatment and what was delivered.

**Response to treatment**

The total CDRS-R scores decreased significantly from pre-intervention to follow-up assessment ($F(1, 12) = 11.76, p < .01$), and 5 (42%) of the 12 participants who completed the follow-up assessment no longer met the criteria for clinically significant depression (CDRS-R score < 36). Scores also decreased significantly for the BDI-II ($F(1, 32) = 11.19, p < .01$) and the HoNOSCA ($F(1, 37) = 4.54, p < .05$) and increased significantly for the IQLC ($F(1, 31) = 5.27, p < .05$). No significant changes were seen on the FBB-DES and the CGI. See Table 4. Furthermore Figure 3 demonstrates the course of the BDI-II assessments per session. Results revealed a decline of symptom severity from session two onwards.

With respect to suicidal ideation, pre-intervention, just 4 (26.7%) participants had a response of “none to mild” on Item 13 of the CDRS-R while 11 (73.3%) had a response of “moderate to severe”. Post Session 5, these numbers were 10 (67%) and 5 (33%), respectively; and at follow-up, they had further improved to 10 (80.0%) and 2 (20.0%), respectively. The change from pre-intervention to follow-up was statistically significant ($F(1, 32.81) = 4.25, p < .05$).

**Discussion**

The aim of this pilot study was to assess a brief cognitive behavioural group therapy programme in adolescent out-
patients suffering from depression. The results showed good feasibility and significant clinical improvements. The adolescents in this programme participated on a regular basis and rarely missed sessions, despite the low level of psychosocial functioning usually associated with a major depressive disorder.

With regard to acceptance, the most positive evaluations were given for being with other adolescents and feeling comfortable in the group. One reason for this could be that compared to their healthy peers, depressed adolescents have more problems with social relationships, fewer contacts with peers, and more likelihood of social rejection [44]. Individuals with depression often have social deficits that weaken their chances for social reinforcement [45]; thus, the opportunity for positive social experiences in a protected setting in which they feel comfortable would be highly important to them. However, considering the drop-outs more closely, it becomes obvious that two of three had a comorbid social phobia. As written in the introduction, the group setting might be overly stressful and less appropriate for them than the individual setting. Participants also reported that they felt understood by and comfortable with the group leaders, and rated their advice as helpful. The importance of a positive therapeutic alliance and its effect on therapeutic outcome has been demonstrated elsewhere [46], and could be a nonspecific factor that at least partly explains the improvement in symptoms.

The least positive evaluations were on whether participants found what they learned in the group to be helpful in their family lives. One reason for this could be that adolescents are at an age where they increasingly detach from their parents while friends become more important. It was notable that only 3 participants chose a parent as the “person of trust” to bring to Session 5 therefore this item might be appropriate for only some of the sample. A further reason could be that one session might not be enough to focus on all skills necessary. The addition of a cognitive behavioural family therapy component [47] might improve response rates.

Furthermore participants rated inclusion of family and friends little helpful. The reason for including the person of trust was to help prevent relapses; however, such assistance may not be necessary until much later. Therefore, assessing the value of this role shortly after completion of the program may not be useful, as the patient is unlikely to require such support at this time. The value of including and training a supportive friend or family member should be evaluated in a longitudinal design.

Adherence to the MICHI protocol was 93%, which is comparable to the range of 80% to 94% reported for other manualised studies [20-23]. The high fidelity of implementation may be attributable to the detailed instructions provided in the treatment manual.

Significant improvements were seen on measures of depression and the pre-post follow-up test comparison revealed a moderate effect size for the CDRS-R and a small effect size for the BDI-II. The remission rate of 42% was slightly lower than the rates of 45.2% and 56.0% seen by Ihle et al. [48,49], who used a similar pre-post design in their investigation of the German version of the “Adolescent Coping with Depression Course (CWD-A)”. It must be noted that the CDW-A programme, while brief, consists of ten 2-hour group sessions in comparison with only six 1.25-hour group sessions in MICHI. In any case, the remission rate in MICHI is within the range (39%–62%) seen with international studies for the evaluation of group treatments for depressed adolescents [22,23,50]. Due to the small number of participants in the present sample, the remission rate needs to be addressed in a larger sample as well.

No significant change was seen in the scores of the parent-rated FBB-DES. This could be explained by the fact that symptoms of depression, such as reduced self-esteem, feelings of depression, guilt and hopelessness, and suicidality, are difficult for parents to observe. This aspect was also reported by Weisz et al. [6], who noted that after therapy of depressed adolescents, the youth-completed reports revealed significant improvement while the parent-completed reports did not. Pre-post follow-up test comparisons in the IQLC and HoNOSCA revealed small effect sizes and the CGI scores improved slightly but not significantly, which again might be a factor of the small number of participants.

There was a significant reduction in the number of participants reporting suicidal ideation within the last 2 weeks, with only 20% still responding “moderate to severe” at follow-up. In a study of healthy European adolescents aged 14–16 years, Resch et al. [51] found that 17% of females and 8.3% of males reported having had
suicidal thoughts within the last 2 weeks, as assessed by the Paykel Scale [52]. Thus, the percentage of adolescents with suicidal ideation seen in our sample follow-up-intervention is not much larger than that seen in a non-clinical population of the same age. This finding of a reduction of suicidal thoughts following outpatient treatment is important, as suicidality in adolescents is a major public health problem due to its frequency, likelihood for recurrence, increased risk for completed suicide, and health costs [53].

A comparison of the results of this pilot study with the earlier pilot study of MICHI in in-patients [17] revealed no difference in feasibility and a nearly identical improvement in pre-post CDRS-R scores. With respect to suicidal ideation, the out-patients showed a higher percentage of moderate to severe suicidal ideation pre-intervention than did the in-patients. Post-intervention, reduction of suicidal ideation was comparable between both samples.

Some limitations of this pilot study must be recognized. These include a small sample size; the absence of a control group, which allows for only weak conclusions about efficacy; a small cronbach’s alpha of the IQLC, which might be due to a small number of items and stronger changes in some items than others, and the inclusion of participants who were receiving medication for depression. We attempted to reduce the impact of medication by including only patients whose regimen was stable for five weeks prior to the start of and during therapy. Furthermore we included participants with co-morbid disorders that could influence results. It is possible that permitting patients to speak to a group leader individually following a session in case of an acute crisis could have influenced results; however, this opportunity was used only few times. This issue was discussed before the start of the programme, and was felt to be a necessary supplement for ethical reasons and because it reflects practical reality.

Conclusions

The results of this pilot study revealed a reduction in depression and suicidal ideation and an improvement of quality of life in adolescent outpatients following participation in a brief manualised CBT group therapy programme. Overall, the findings support the feasibility of proceeding with an investigation of the MICHI programme using a larger sample size in a randomized controlled trial design. If the findings are borne out in a controlled trial, this approach could come to be considered a first-line treatment for adolescents with depression, reserving longer-lasting therapies or medical treatment only for those who fail to respond.

Competing interests

All authors declare no conflict of interests.

Authors’ contributions

PLP is PI in a study for Lundbeck. He has received research grants from the BMBF (German Ministries for Research and Education) and the BARM (German Federal Institute for Drugs and Medical Devices) and the state foundation (Landesstiftung) Baden-Württemberg. He has received travel grants from the DFG, DAAD and JACAPAP. He is not a shareholder in the pharmaceutical industry. JS managed the literature searches, acquisition of data, and analysis and interpretation of data, and was the primary author of the article. NS developed the MICHI training manual and designed the study. PLP aided in the literature search. MB conducted group therapy sessions and helped with acquisition of data. MK supervised and coordinated the study. All authors contributed to the manuscript and approved the final version. JMF has received research funding in the last 5 years from EU, DFG, BMG, BMBF, BMBF, several state ministries of social affairs, State Foundation BaWue, Volkswagen Foundation, European Academy, Gregororian University, Vatican, RAZ, CID, Eli Lilly research foundation, Janssen-Cilag (J&J), Medice, Celtech/CUB, Furthermore, he has received travel grants, honoraria, and sponsoring for conferences and medical educational purposes from DFG, AACAP, NIMH/VH, EU, the Vatican, Goethe Institute, Pro Helvetia, Asta, Aventis, Bayer, Bristol-MS, Celtech/CUB, Janssen-Cilag (J&J), Lilly, Medice, Novartis, Pfizer, Ratiopharm, Sanofi-Synthelabo, Shire, VFA, Generika Verband, several universities and professional associations, and German federal and state ministries. MGK has received unrestricted grants from Eli Lilly International Foundation. He has received research grants from the BMFSJ (German Ministries for Family Affairs, Senior Citizens, Women and Youth), the BMBF (German Ministries for Research and Education), the Schweizer Bundesamt fuer Justiz, and Boehinger Ingelheim. He has been a CI or PI for Eli Lilly, Astra Zeneca, and Janssen-Cilag, Lundbeck. He has received travel grants or payments for lectures from Janssen-Cilag, the University of Rostock, DGKPP, CUB, Europaeische Akademie and from various non-profit organizations. He is not a shareholder in the pharmaceutical industry.

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References

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6.8 MICHI – a brief, manualized cognitive behavioural group therapy for the treatment of depression in adolescents: randomized controlled trial.

Contribution of J. Straub to the article:
J. Straub coordinated the study procedure and recruited participants. She executed weekly group therapy sessions, assessed suicidal ideation and behaviour on a weekly basis, and scheduled diagnostic as well as psychotherapeutic appointments. She controlled the return of questionnaires and executed diagnostic assessments that didn't have to be done by an independent evaluator (e.g. IQ measurements). She did data acquisition, generated the data matrix, did data input, executed statistical analyses, and interpreted statistical outcomes. She researched literature, wrote the manuscript, integrated remarks of the co-authors, revised the manuscript according to reviewer’s comments, and created figures and tables.

Co-author’s contribution to the article:
N. Sproeber and M.G. Koelch supervised decisions on the experimental design and conceptualized the study. They supervised the conduction of weekly group therapy sessions. They reviewed the draft and gave constructive remarks and helped with revising the manuscript according to the reviewer’s comments. F. Keller helped with statistical analyses. P.L. Plener, F. Keller and J.M. Fegert reviewed the draft and gave constructive remarks.

Reference

MICHI – eine Gruppen-Kurzzeitpsychotherapie zur Behandlung von Depressionen bei Jugendlichen

Eine Randomisierte kontrollierte Studie

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MICHI – A Brief, Manualized Cognitive Behavioral Group Therapy for the Treatment of Depression in Adolescents: A Randomized Controlled Trial

Abstract. Cognitive behavioral psychotherapy (CBT) is one of the first choices for the treatment of depression in adolescents but to date no German treatment program has been evaluated in a randomized controlled trial. The study comprised 38 depressed adolescents (M = 15.86; SD = ±1.70 years old; 78.9% girls) who were randomly assigned to a control group (CG), a group that received treatment as usual (TAU), or an intervention group (IG) that participated in a brief outpatient group CBT called MICHI. To determine treatment efficacy, changes in the CDRS-R and BDI-II scores before and after TAU or CBT were collected and compared between groups. The interaction effects, of groups and time points, were significant (p < .02) for the CDRS-R, with a moderate effect size (d_korr=.75), and for the BDI-II (p < .04), with a small effect size (d_korr=.39). The results of the present study reveal that a brief CBT, in a group format, was significantly more effective than TAU. Keywords: depressive episode, adolescents, cognitive behavioral psychotherapy, group therapy

Im Grundschulalter wird die Lebenszeitprävalenz, für die Entwicklung einer depressiven Episode, auf 1–2% bei gleicher Geschlechterverteilung geschätzt (Groen & Pettermann, 2008). Im Jugendalter liegt die Prävalenz für depressive Störungen (laut Meta-Analyse unter Berücksichtigung verschiedener Diagnostik-Zeitraume) bei 5,6% (Costello, Erkanli & Angold, 2006) und Mädchen sind mit 9,7% (Punktprävalenz) doppelt so häufig betroffen wie Jungen mit 4,7% (Bettge et al., 2008). Neben dem Symptom der Suizidalität, immerhin die zweithäufigste Todesursache im Jugendalter (Wilkinson, Kelvin, Roberts, Dubicka & Goodyer, 2011), besteht die Notwendigkeit einer effektiven, zielführenden Behandlung bereits im Jugendalter, um die entsprechende Dauer der Episode so kurz wie möglich zu halten.

Die Deutsche Leitlinie zur Behandlung von depressiven Störungen bei Kindern und Jugendlichen (2013) empfiehlt, dass bei älteren Kindern und Jugendlichen mit leichter bis mittelgradiger depressiver Episode die Psychotherapie Vorrang zu geben sei und dabei entweder eine kognitiv-verhaltenstherapeutische (KVT) oder interpersonelle Psychotherapie (IPT) zum Einsatz kommen solle (Evidenzgrad A). Da bisher kaum deutsche Behandlungsprogramme untersucht wurden, davon keines im randomisierten kontrollierten Design (Deutsche Gesellschaft für Kinder- und Jugendpsychiatrie, 2013), basieren diese Empfehlungen primär auf Meta-Analysen, welche englischsprachige Wirksamkeitsstudien zur Therapie von Depressionen bei Kindern und Jugendlichen berücksich-

Nina Spröber und Michael G. Kölch teilen sich die Letztautorenchaft.

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tigen. Seit dem Jahr 2000 wurden diesbezüglich neun Meta-Analysen veröffentlicht (Compton et al., 2004; David-Ferdon & Kaslow, 2008; Erford et al., 2011; Klein, Jacobs & Reinecke, 2007; McDermut, Miller & Brown, 2001; Michael & Crowley, 2002; Spielmans, Pasek & McFall, 2007; Watanabe, Hunot, Omori, Churchill & Furukawa, 2007; Weisz, McCarty & Valeri, 2006), die eine psychotherapeutische Intervention, zumeist KVT und IPT, mit einer aktiven, inaktiven oder Wartelisten-Kontrollgruppe verglichen. Je Meta-Analyse wurden gemittelt 20,56 (SD=9,15) Studien eingeschlossen. Die Effektstärken lagen zwischen 0,29 (Erford et al., 2011) und 1,03 (McDermut et al., 2001) mit einer mittleren Effektstärke von 0,58 (SD=0,30), wobei nicht alle Studien eine Effektstärke berichteten (Erford et al., 2011; Klein et al., 2007; McDermut et al., 2001; Michael & Crowley, 2002; Weisz et al., 2006) (für einen Überblick zu aktuellen Meta-Analysen s. auch Groen & Petermann, 2012).


Methoden
Prozedere

tiktermin eingeladen bei welchem das Vorliegen gegen-
wärtiger psychischer Störungen mittels klinischem Inter-
view, sowie eine Erfassung des Intelligenzniveaus vorge-
nommen wurde.

Die randomisierte kontrollierte Studie wurde in fünf Durchgängen von September 2011 bis Oktober 2013 durchgeführt. Je Durchgang wurden ca. acht depressive Jugendliche randomisiert entweder der Interventions-
gruppe (IG) oder der Kontrollgruppe (KG) zugeordnet. Anschließend folgte jeweils ein fünfwöchiger Zeitraum, in welchem die IG wöchentlich eine Sitzung MICHI und die KG TAU erhielt. Dann folgte eine post-Diagnostik und die IG erhielt fünfeinhalb Wochen nach den fünfzehn MICHI-Sitzung eine Auffrischungssitzung. Fünf Wochen nach der post-Diagnostik nahm die Interventionsgruppe an der Nachuntersuchungs-Diagnostik teil.

Aus ethischen Gründen wurde in beiden Gruppen eine mögliche Verschlechterung der Symptomatik und Suizidalität erfasst: Der BDI-II wurde von den Jugendlichen der IG nach jeder Sitzung erhoben, bei den Jugendlichen der TAU Gruppe wöchentlich. Wurde Item 9 des BDI-II, welches akute Suizidalität erfragt, mit 2 („ich möchte mich am liebsten umbringen“) oder höher angegeben, wurde der Ju-
gendliche umgehend kontaktiert und zu einem Gespräch eingeladen bzw. es erfolgte nach der Sitzung ein Einzelges-
spräch, um die Schwere und Akuität der Suizidalität und das notwendige weitere klinische Prozedere klären zu können.

Die Studie wurde von der Ethikkommission der Uni-
viersität Ulm begutachtet, und Teilnehmer und ihre Sor-
geberechtigten wurden vor Studienbeginn über die Stu-
dienteilnahme mündlich wie schriftlich informiert und un-
terzeichneten anschließend die Einverständniserklä-
rung für die Studienteilnahme. Aus ethischen Gründen
bestand für die Jugendlichen der KG die Möglichkeit, im Anschluss an den Wartezeitraum mit TAU ebenso an MICHI teilzunehmen.

Teilnehmer

Einschlusskriterien waren ein Alter zwischen 13 und 18 Jahren, ein IQ größer 80, die Diagnose einer leichten, mit-
telgradigen oder schweren depressiven Episode nach klini-
schem diagnostischen Interview „Kiddie Schedule for Af-
fector Disorders and Schizophrenia, Present and Lifetime Version (K-SADS-PL)“ (Kaufman, Birmaher & Brent, 1997) sowie ein Summenwert ≥ 36 in der Children’s Depression Rating Scale Revised (CDRS-R) (Keller, Grieb, Koechle & Sproeber, 2012; Poznanski & Mokros, 1996) wie er auch z.B. in der „The Treatment of Adolescent Suicide Attempts study (TASA)“- Studie herangezogen wurde (Brent et al., 2009). Acht Jugendliche wiesen einen CDRS-R Wert ≤36 auf, wovon vier zudem nicht die Kriterien einer depressiven Episode im K-SADS-PL erfüllten, und konnten daher nicht in die Studie eingeschlossen werden (s. Abbil-
dung 1). Um eine für den klinischen Alltag möglichst re-
präsentative Stichprobe zu erhalten, wurden auch Jugend-
liche mit komorbidem Störungen eingeschlossen, die depres-
sive Störung (ICD F32, F33) sollte allerdings im Vorder-
grund stehen und die vorrangige Störung sein, weshalb kinder- und jugendpsychiatrische/-psychotherapeutische Hilfe aufgesucht wurde. Jugendliche, die gegenwärtig die Kriterien einer bipolaren Störung, Schizophrenie oder Suchterkrankung erfüllten, wurden nicht in die Studie eingeschlossen, da bei diesen Störungsbildern eine andere Be-
handlung vorrangig indiziert ist. Einnahme von Medikation
wurde erlaubt, insofern diese mindestens fünf Wochen vor Therapiebeginn begonnen wurde und es keine Änderung in der Dosierung während der Studienteilnahme gab. Sowohl die Teilnehmer als auch ihre Erziehungsberechtigten wurden gebeten, eine etwaige Änderung der Medikation oder den Beginn einer anderweitigen Psychotherapie mitzuteilen, da ihre Daten dann nicht in die Studie einbezogen werden könnten, dies jedoch nicht zu einem Ausschluss aus der Therapie führen würde. Für die Teilnehmer der IG gilt dar-
über hinaus, dass sie mindestens vier von sechs Sitzungen (67%) besuchen mussten, da ihre Werte ansonsten als Drop-
outs in die Analysen eingingen.

Interventionen

Grundlegende Behandlungselemente von MICHI sind: (1) Psychoedukation, (2) kognitive Umstrukturierung, (3) Verhaltensaktivierung, (4) Ressourcenaktivierung, (5) Steigerung des Selbstwertgefühls, (6) schrittweises Problemlösen, (7) Emotionsregulation, (8) Krisemanage-
ment (9) und Rückfallprophylaxe (für einen Überblick über die konkreten Sitzungsinhalte s. Sproéber et al., 2012). Die fünf Sitzungen plus eine Auffrischungssitzung wur-
den in Kleingruppen von 4–6 Teilnehmern abgehalten.

Die fünf Sitzungen dauerten zwischen 65–90 Minuten (M=74,78; SD=9,57) und wurden von zwei Co-Autoren des Manuale, beides klinische Psychologinnen, durchge-
führt. Um eine bestmögliche Behandlungsintegrität zu errei-
chen, arbeiteten die Therapeuten nach Trainer-Manu-

ual (Sproéber et al., 2012) und erhielten zudem eine
Checkliste mit den jeweiligen Sitzungsinhalten. Außer-
dem wurden sie in der Durchführung der Sitzungen vorab geschult und wöchentlich von der Entwicklerin des Ma-
tuals supervidiert. Zur Erfassung der Behandlungsinte-
grität wurden alle Sitzungen auf Video aufgezeichnet, 25 % der Sitzungen randomisiert ausgewählt (N=15) und

anhand einer Checkliste, von einer klinischen Psycholo-
gin, die unabhängig von der Studien- und Therapie-
durchführung war, auf Durchführungs-Integrität hin überprüft. Diese betrug 98,24 % in der vorliegenden Studi-
e. Jugendliche der KG erhielten kinder- und jugend-
psychiatrische Regelversorgung, welche für den Warte-
kontrollgruppenzeitraum aus 1,74 (SD=1,35) Terminen.
Erhebungsinstrumente


Die Durchführung fand bei der prä-Messung, post-Messung und im Falle der IG auch bei der Nachuntersuchung statt. Beim CDRS-R handelt es sich um ein semi-strukturiertes klinisches Interview welches von für die Gruppenzugehörigkeit (IG, KG) verbindeten, klinischen Psychologen durchgeführt wurde. Ein Wert von ≥36 liefert Hinweise auf eine klinisch bedeutsame Symptomatik (Plener et al., 2012). Sowohl die CDRS-R (α=,85) (Keller et al., 2011) als auch das BDI-II weisen eine gute interne Konsistenz (,89≤α≤,94) (Beck et al., 1996; Hautzinger et al., 2006) auf. Um eine Veränderung der Suizidalität erfassen zu können, wurde das CDRS-R Item 13 im klinischen Interview herangezogen, welches eine Einstufung der Suizidalität in „keine bis leichte“ sowie „moderate bis schwere“ Suizidalität über die letzten zwei Wochen ermöglicht.

Stichprobengröße

Die Stichprobengröße wurde vorab anhand von Power-Analysen bestimmt. Dabei wurde von einer Teststärke 1-β≥,80, einem Risiko für Fehler 1. Art α=.05 und einer erwarteten mittleren Effektstärke von d=.50 ausgegangen. Es wurde eine Mindestteilnehmerzahl von N=34 (17 Teilnehmer pro Gruppe) festgelegt.

Randomisierung


Statistisches Vorgehen


Resultate

Charakteristika der Teilnehmer

38 Jugendliche erfüllten die Einschlusskriterien und wurden randomisiert der IG oder KG zugeordnet. Durchschnittlich besuchten die Teilnehmer der IG 5,39 (SD=,70) Sitzungen von sechs. In der KG erhielten die Jugendlichen durchschnittlich 1,74 (SD=1,35) Termine während des fünfwöchigen Kontrollzeitraums. Zwei Teilnehmer der KG und ein Teilnehmer der IG verließen das Studienprotokoll von pra nach post (Änderung der stabilen Medikationseinnahme; Beginn einer Psychotherapie) und zwei Teilnehmer der IG verließen das Studienprotokoll von post zur Nachuntersuchung (Änderung der stabilen Medikationseinnahme) (s. Abb. 1).

Nach Studienteilnahme gaben 13 der 19 Jugendlichen der IG an, weiterhin sozialpsychiatrisch angebunden zu bleiben und zwei der Jugendlichen gaben an, eine wöchentliche Psychotherapie beginnen zu wollen.

Die Gruppen unterschieden sich nicht hinsichtlich Alter, Geschlecht und IQ. Auch die Anzahl an Jugendlichen mit Migrationshintergrund sowie Jugendliche, bei denen im Verlauf akute Suizidalität abgeklärt werden musste, unterschied sich kaum. In der KG waren mehr Gymnasiasten und die Verteilung der Depressions-Schweregrade etwas ausgewogen verteilt wobei sich der Schweregrad, gemessen anhand des CDRS-R, beiden Gruppen nicht unterschied (s. Tab. 1).
Veränderung der depressiven Symptomatik

Nach Teilnahme an MICHI wies die Hälfte der Teilnehmer (N=9) der IG einen CDRS-R Wert unter 36 (Cut-Off Wert) im Vergleich zu fünf Teilnehmern der KG auf. Die Mittelwerte unterschieden sich bei der prä-Messung zwischen beiden Gruppen weder hinsichtlich der CDRS-R (*t*(36)=,.04, *p*=.97) noch dem BDI-II (*t*(36)=-.79, *p*=.44) signifikant, d.h. die beiden Gruppen waren in ihrer Depressivität vergleichbar. Über die Auswertung mit dem HLM zeigten sich signifikante Haupteffekte für den Faktor Messzeitpunkt in der CDRS-R und dem BDI-II und keine signifikanten Haupeffekte für den Faktor Gruppe. Bezüglich der Interaktionseffekte Gruppe x Messzeit-

Anmerkungen: N=Anzahl Teilnehmer; CDRS-R=Children’s Depression Rating Scale Revised; IG=Interventionsgruppe; KG=Kontrollgruppe; TAU= Treatment As Usual; MICHI=Manualized Intervention to Cope with depressive symptoms, Help strengthen resources and Improve emotion regulation; HLM=Hierarchisch lineares Modell; LOCF=last observation carried forward; MZP=Messzeitpunkte.

Abbildung 1. Flow-Chart.
punkt ergaben sich signifikante Effekte für die fremdbeurteilte (CDRS-R), mit einer mittleren Effektstärke, sowie für die selbstbeurteilte (BDI-II) Depressivität mit einer kleinen Effektstärken (s. Tab. 2). Die Betrachtung der post-Nachuntersuchungsergebnisse zeigte, dass die während der Therapiephase erzielte Symptomreduktion im
Nachuntersuchungszeitraum von fünf Wochen stabil blieb (s. Abb. 2).

Veränderung der Suizidgedanken

Sowohl in der IG als auch KG kam es aufgrund von Angaben im BDI-II Fragebogen oder im CDRS-R Interview zur Abklärung akuter Suizidgedanken (Häufigkeit von Suizidgedanken je Gruppe s. Tab. 1). Dabei kam es aus- schließlich zu Suizidgedanken, von denen sich der jeweilige Patient in der individuellen Abklärung und einem kurzen Einzelgespräch glaubhaft distanzieren konnte; von einer stationären Aufnahme konnte bei allen Teilnehmern abgesehen werden.

Vor Teilnahme an MICHI berichteten zehn Jugendliche, direkt nach Teilnahme vier Jugendliche und bei der Nachuntersuchung sechs Jugendliche von moderaten bis schweren Suizidgedanken über die vergangenen zwei Wochen hinweg. Es zeigte sich eine deutlich signifikante Abnahme der Suizidgedanken in der IG und keine signifikante Abnahme in der KG gemessen anhand des CDRS-R Items 13, wobei die Interaktion nicht signifikant wurde (s. Tab. 2).

Ausschluss medizierter Patienten

Auch nach Ausschluss der jeweils drei medizierten Patienten der IG und KG blieben die Interaktionseffekte für den CDRS-R ($F(1.30)=4.09$, $p=.05$), BDI-II ($F(1.28)=5.53$, $p=.03$) und CDRS-R Item 13 ($F(1.30)=.29$ $p=.59$) vergleichbar mit den Ergebnissen aller Patienten.

Diskussion

In der vorliegenden Studie konnte gezeigt werden, dass eine Gruppen-Kurzzeitintervention von nur fünf Sitzungen gegenüber Behandlung wie üblich effektiv war. Sowohl im Kliniker- als auch Selbsturteil zeigte sich ein signifikanter Interaktionseffekt zwischen Messzeitpunkten die Gruppen mit kleinen bis mittleren Effektstärken. Suizidgedanken verringerten sich in der IG signifikant, jedoch ohne signifikanten Interaktionseffekt.


Darüber hinaus bleibt zu diskutieren, warum sich auch in der KG Depressionswerte im Verlauf signifikant verringerten. Dies lässt sich zum einen durch die Tatsache, dass auch die KG Behandlung wie üblich erhielt, sowie zum anderen durch eine hohe Spontanremissionsrate depressiver Störungen im Kindes- und Jugendalter (Whiteford et al. 2012) erklären.


Limitationen der vorliegenden Studie sind zum einen der geringe Anteil an männlichen Teilnehmern, was die Generalisierbarkeit der Daten auf das männliche Geschlecht einschränkt. Dabei ist allerdings anzumerken, dass die Geschlechterverteilung in der vorliegenden Studie vergleichbar mit der Prävalenz depressiver Störungen beider Geschlechter ist. Weiterhin wurden in der vorliegenden Studie teilweise medizierte Patienten eingeschlossen, wobei sich die Ergebnisse, bei Ausschluss der medizinierten Patienten, kaum änderten. Auch wenn sich die CDRS-R Rohwerte beider Gruppen zu Beginn nicht unterschieden, wies die KG einen höheren Anteil an Jugendlichen mit schweren depressiven Episoden auf (erfasst anhand des K-SADS-PL). Darüber hinaus erhielt die KG durchschnittlich 1,74 Termine in der kinder- und jugendpsychiatrischen Versorgung, wobei die Kriterien für eine objektive Vergleichsgruppe, im strengen Sinne der empirischen Wirksamkeitsforschung, nicht erfüllt waren. Nichtsdestotrotz bildet dieses Vorgehen aus unserer Sicht die kinder- und jugendpsychiatrische Praxis am besten ab. In der Studie wurde ein primäres Zielkriterium gewählt, welches die depressive Symptomatik fokussiert. Möglich wäre es weitere Aspekte, wie das psychosoziale Funktionsniveau heranzuziehen, was in weiteren Studien anzustreben wäre.

In weiterführenden Studien sollte die Wirksamkeit von MICHI gegenüber einer Kontrollintervention im Längsschnittdesign mit einer späteren Nachuntersuchung (z. B. nach sechs Monaten) erfasst werden, um das langfristige Anhalten des Effekts überprüfbar zu können. Weiterhin wäre es sinnvoll, die Wirksamkeit von MICHI in einer größer angelegten multizentrischen Studie, gegebenenfalls auch im Vergleich zu einer medikamentös behandelten Vergleichsgruppe, zu untersuchen.

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Neural correlates of successful psychotherapy of depression in adolescents

6.9 Neural correlates of successful psychotherapy of depression in adolescents

Contribution of J. Straub to the article:

J. Straub coordinated the study procedure and recruited participants. She executed weekly group therapy sessions, assessed suicidal ideation and behaviour in the patients on a weekly basis, and scheduled diagnostic as well as psychotherapeutic appointments. She controlled the return of questionnaires and executed diagnostic assessments that did not have to be done by an independent evaluator (e.g. IQ measurements). With the technical assistance of K. Braendle and E.-J. Sim she executed fMRI scans. She performed data acquisition, generation of the data matrix, data input and execution of statistical analyses regarding clinical, behavioural, and fMRI data. She interpreted statistical and neuroimaging outcomes. She researched literature, wrote the manuscript, integrated remarks of the co-authors, revised the manuscript according to reviewer’s comments, and created figures and tables.

Co-authors’ contributions to the article:

B. Abler made decisions on the experimental design, conceptualized the study, and supervised the writing of the proposal for the ethical committee. She supervised the coordination of study procedures, fMRI measurements, configuration of diagnostic instruments, pre-processing of fMRI data, and higher level analyses by means of SPM. She provided literature, supervised and helped with writing the manuscript, as well as integrating the remarks of co-authors and reviewers comments. P.L. Plener helped conceptualize the study, provided literature and made constructive remarks on the manuscript. N. Sproeber helped conceptualize the study, helped with coordinating the study procedure and the configuration of diagnostic instruments, and supervised the weekly group psychotherapy. L. Sprenger helped conceptualize the study, wrote the proposal for the ethical committee, reviewed the draft, and gave constructive remarks. M. Koelch decided on experimental design and conceptualisation of the study, helped coordinate study procedure, reviewed the draft, and gave constructive remarks. G. Groen supported study conceptualisation and higher level analyses of functional brain imaging data by means of SPM. He helped with writing the manuscript as well as integrating the remarks of co-authors and reviewer’s comments.

Reference


Research report

Neural correlates of successful psychotherapy of depression in adolescents

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A B S T R A C T

Background: While major effort has been put in investigating neural correlates of depression and its treatment in adults, less is known about the effects of psychotherapy in adolescents. Given the concordance of the ventral striatum, amygdala, hippocampus and the subgenual anterior cingulate cortex (sgACC) as correlates of depression and their involvement in reward processing, we used functional magnetic resonance imaging (fMRI) during performance of a monetary reward task in an intervention versus waitlist-control design to investigate the clinical and neural effects of cognitive behavioral group therapy (CBT-G).

Methods: 22 medication naïve adolescents with major depressive disorder were scanned before and after five sessions of CBT-G (PAT-I), or before and after five weeks of waiting (PAT-W). Changes in symptom scales were analyzed along with neural activation changes within the amygdala, hippocampus, sgACC and ventral striatum regions of interest (ROI).

Results: Psychometric assessments and ROI activation remained unchanged in PAT-W. In PAT-I, significant reduction in clinical symptoms accompanied significant changes in brain activation within the left amygdala, left hippocampus and bilateral sgACC. In line with previous findings in adults, pre-to-post-activation changes in the bilateral sgACC correlated with pre-to-post and pre-to-follow-up symptom improvement, and individual expressions of sgACC activation before treatment were related to pre-to-follow-up therapeutic success.

Limitations: Future studies should include larger sample sizes.

Conclusions: Successful group psychotherapy of depression in adolescents was related to signal changes in brain regions previously demonstrated to be reliably linked with successful, particularly pharmacological treatment in adults.

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1. Introduction

Given the increased risk for the development of affective disorders in youth (Duggal et al., 2001), with a raising number of incidents (Ryan et al., 1992), and the risk for relapses in adulthood (Patton et al., 2014) effective therapies for depressed adolescents are needed (Jonsson et al., 2011). Understanding the neural correlates of adolescent depression may assist in better shaping of therapies to the special characteristics and needs of this particular group of patients. Furthermore, investigating the neural correlates of psychiatric disorders in adolescents offers the opportunity to research a disorder at an early stage, thus bypassing otherwise relevant effects of previous medication and/or by changes in neural processing due to a chronic course of the disorder like in studies with adults (Cullen, 2012).

Research on regional brain activity modulated by depression showed a particularly consistent pattern of involvement of the amygdala, hippocampus, subgenual anterior cingulate cortex (sgACC), and ventral striatum for both adults and adolescents (Arnone et al., 2012, Forbes et al., 2009, Fu et al., 2008, Godlewksa et al., 2012, Goldapple et al., 2004, Gotlib et al., 2005, Hall et al., 2014, Kennedy et al., 2001, Mayberg et al., 2000, Sheline et al., 2001, Yang et al., 2010). In adults, pre-to-post-comparisons of the effect of antidepressant medication reliably showed a reduction of amygdala reactivity (Arnone et al., 2012, Godlewksa et al., 2012, Sheline et al., 2001). Likewise, pharmacological pre-to-post-modulation of activations of the hippocampus and sgACC has been repeatedly reported, although the direction of activity changes was less consistent as compared to results for the amygdala (Kennedy...
et al., 2001, Mayberg et al., 2000). Some evidence supports similar effects for psychotherapeutic interventions in adults (Fu et al., 2008, Goldapple et al., 2004). For example, two previous studies have shown that pre-treatment activity in the sgACC was associated with subsequent psychotherapeutic treatment response in adults (Siegle et al., 2006, 2012), which is in line with the notion that the sgACC seems to be a key structure for emotional processing (Thomason et al., 2011).

Treatment effects in depressed adolescents are much less investigated. Some evidence supports consistency with studies in adults with modulation of activity levels in the sgACC and amygdala by antidepressant medication (Tao et al., 2012). However, effects of psychotherapy in adolescents with depression still await further empirical investigation. To probe the modulation of the activation of amygdala, hippocampus, sgACC and ventral striatum by a psychotherapeutic intervention in depressed adolescents, we used functional magnetic resonance imaging (fMRI) of a reward paradigm. Selection of this paradigm was mainly motivated by the empirical observation from previous studies (Forbes et al., 2009, Haber and Knutson, 2010) that these core regions associated with reward processing as a candidate endophenotype of depression (Elliott et al., 1997). This may explain why patients tend to overestimate failure and punishment, and tend to underestimate success and positive reinforcement (Elliott et al., 1997).

Given previous results from intervention studies in adults with depression (Fu et al., 2008, Goldapple et al., 2004) we expected that positive psychotherapeutic treatment effects would be accompanied by significant activity changes in the amygdala, hippocampus, sgACC and ventral striatum in depressed adolescents. Furthermore, we hypothesized that pre-treatment neural activity in the sgACC would correlate with individual symptom improvement (Siegle et al., 2006). Signal and symptom changes of patients receiving therapeutic treatment were furthermore expected to differ from patients in a waiting group.

2. Methods

2.1. Participants

22 medicated naïve adolescents (17 females; five males), between 13 and 18 years of age ($M = 16.47, SD = 1.36$), diagnosed with major depressive disorder according to DSM-IV and with a raw sumscore $\geq 36$ (Plener et al., 2012) in the Children’s Depression Rating Scale Revised (CDRS-R) (Keller et al., 2012) were included into the study. All participants were outpatients of the Department of Child and Adolescent Psychiatry and Psychotherapy of the local university. Exclusion criteria were a current or previous diagnosis of bipolar disorder, schizophrenia or substance abuse, IQ < 80, major somatic or neurological disorders and general contradictions to MRI scanning such as braces, metallic implants, or pregnancy. All participants and their caregivers provided written informed consents and the study was approved by the Institutional Review Board of Ulm University.

2.2. Procedures

Each subject received a psychological assessment upon inclusion to the study to evaluate psychiatric status and intelligence. Eligible patients were assigned to a group receiving psychotherapeutic intervention PAT-I (N = 10) or a waiting group PAT-W (N = 12). Functional MR imaging was performed before and after five weeks of intervention that comprised weekly sessions of a cognitive behavioral group therapy (CBT-G), and before and after five weeks of waiting, comprising appointments with a psychiatrist/psychologist once to three times within three months for approximately 30 min. The MICHI intervention and appointments with psychiatrist/psychologist, were comparable irrespective of waiting or of not waiting before. Five weeks after the end of the intervention, a booster therapy session was applied to patients of PAT-I. The first scan and psychometric assessment of depression (pre-waiting/pre-intervention) took place within 10 days before waiting or intervention. Post-waiting and post-intervention MR scans as well as psychometric assessment of depression took place within 10 days after completion of the five weeks periods. After the booster session another psychometric assessment of depression (follow-up-intervention), but no further fMRI imaging took place (see Fig. 1).

![Fig. 1. Study design. PAT-W= depressed patients of the waiting group (N=12); PAT-I= depressed patients that participated in MICHI (Manualized Intervention to Cope with depressive symptoms, Help strengthen resources and Improve emotion regulation, N=10); PAT-I complete (N=18) encompasses all patients of PAT-I and eight patients of PAT-W that received psychotherapeutic intervention after their waiting period for ethical reasons. Psychological assessment included CDRS-R (Children’s Depression Rating Scale Revised) and BDI-II (Beck Depression Inventory Revision).](image-url)
Eight of the 12 participants initially assigned to PAT-W were also allowed to participate in the intervention after waiting for ethical reasons. Together with PAT-I (N = 10), a total of 18 subjects received the intervention (PAT-I complete). All subjects in PAT-I complete received the same treatment irrespective of having been assigned directly to PAT-I or to the waiting group before the intervention. Associations between individual symptom improvement and subsequent changes of neural activity were calculated within the PAT-I complete group. Longitudinal effects (pre-to-post, post-to-follow-up and pre-to-follow-up therapy) were assessed in the PAT-I and PAT-W groups.

The mean pre-test CDRS-R score was 56.11 (SD = 9.11) for PAT-I complete. Mean pre-test CDRS-R score (M = 56.70, SD = 11.28) for PAT-I (N = 10) was numerically comparable, and did not differ from the mean pre-test CDRS-R score (M = 54.92, SD = 11.40, t(20) = 0.37, p < 0.72) of the PAT-W group.

Additional analyses revealed, that post-waiting scores of PAT-W, before consecutive admission to MICHI (N = 8), did not differ significantly from pre-intervention scores of PAT-I (N = 10), with neither respect to CDRS-R (t(16) = 0.67, p < 0.51) nor BDI-II (t(16) = 0.47, p < 0.47).

Furthermore, no differences were found with respect to age, sex, IQ, smoking behavior and diagnoses between the PAT-W and both representations of PAT-I (see Table 1).

### 2.4. Psychological assessment

Before inclusion into the study the psychiatric status was assessed by means of the Kiddie Schedule for Affective Disorders and Schizophrenia, Present and Lifetime Version (K-SADS-PL) (Kaufman et al., 1997), and intelligence was assessed by means of either the Wechsler Intelligence Scale for Children-Fourth Edition (WISC IV), Wechsler Adult Intelligence Scale (WAIS) or the testing system for educational counseling (PSB). The choice of the intelligence test depended on age of participants and whether it was possible to arrange a group assessment or not. Upon each fMRI scan (pre-post-waiting and pre-post-intervention) and at follow-up, the change in depressive symptoms was assessed by means of the CDRS-R (Keller et al., 2012) and the Beck Depression Inventory Revision (BDI-II) (Beck et al., 1996, Hautzinger et al., 2006) capturing symptoms during the last two weeks. Diagnostics were done by trained clinical psychologists not involved in the interventional aspect of the study and blinded for group assignment.

Within each group, one-sample t-tests were computed to test whether pre-to-post-intervention or pre-to-post-waiting differences were different from zero to infer significant symptom change over time. Within the PAT-I complete group, a one-sample t-test was also computed to test on differences from zero regarding pre-to-post, pre-to-follow-up, and post-to-follow-up. To infer the significance of treatment effects, pre-to-post-clinical symptom changes were propagated to two-sample t-tests testing on significant interactions of group (PAT-I/PAT-W) and time (pre/post). Statistical analyses were performed using Statistical Package for the Social Sciences 21 (SPSS 21, IBM, Armonk, NY, USA).

### Table 1

Demographics and behavioral data for PAT-I (N = 10), PAT-W (N = 12) and PAT-I complete (N = 18). The lattercompasses all patients of PAT-I (N = 10) and eight patients of PAT-W that received psychotherapeutic intervention after their waiting period for ethical reasons.

<table>
<thead>
<tr>
<th></th>
<th>PAT-I complete (N = 18)</th>
<th>PAT-I (N = 10)</th>
<th>PAT-W (N = 12)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>16.66 ± 1.37</td>
<td>16.39 ± 1.58</td>
<td>16.54 ± 1.21</td>
<td>n.s.</td>
</tr>
<tr>
<td><strong>Handedness</strong></td>
<td>15 females (83.3%)</td>
<td>8 females (80%)</td>
<td>9 females (75%)</td>
<td></td>
</tr>
<tr>
<td><strong>IQ</strong></td>
<td>100.00 ± 8.72</td>
<td>100.00 ± 8.72</td>
<td>99.67 ± 7.55</td>
<td>n.s.</td>
</tr>
<tr>
<td><strong>Depression subtypes</strong></td>
<td>Depressive disorder, mild (N = 3); moderate (N = 11); severe (N = 4)</td>
<td>Depressive disorder, mild (N = 2); moderate (N = 7); severe (N = 1)</td>
<td>Depressive disorder, mild (N = 4); moderate (N = 5); severe (N = 3)</td>
<td></td>
</tr>
<tr>
<td><strong>Secondary diagnosis</strong></td>
<td>Social phobia (N = 4); specific phobia (N = 1); socialized conduct disorder (N = 1); Attention deficit without hyperactivity (N = 1)</td>
<td>Social phobia (N = 2); attention deficit without hyperactivity (N = 1)</td>
<td>Social phobia (N = 2); specific phobia (N = 1); socialized conduct disorder (N = 1)</td>
<td></td>
</tr>
<tr>
<td><strong>Lifetime history of psychotherapy/medication</strong></td>
<td>Psychotherapy (N = 2), Methylphenidate (N = 4)</td>
<td>Psychotherapy (N = 1), Methylphenidate (N = 3)</td>
<td>Psychotherapy (N = 2), Methylphenidate (N = 1)</td>
<td></td>
</tr>
<tr>
<td><strong>Smoker</strong></td>
<td>7 (38.9%)</td>
<td>5 (50%)</td>
<td>3 (25%)</td>
<td></td>
</tr>
</tbody>
</table>

Notes: n.s. = not significant.

a Independent sample t-test; significances were calculated between PAT-I (N = 10) and PAT-W (N = 12).

b Edinburgh Handedness Inventory.

c Diagnosis according to DSM-IV/ICD-10.

d Psychological treatment and previous medical treatment relate to time periods where adolescents were initially treated outside the Department for Child and Adolescent Psychiatry and Psychotherapy without success or with very limited success only.
2.5. fMRI paradigm

We used a well-established monetary incentive task (Abler et al., 2006, 2009) with parametric variation of probabilities (0%, 25%, 50%, 75%, 100%) to win a fixed amount of money (1€). Compared to our previous studies with adults, we had to adapt a maximum amount of money to win in line with the guidelines of the ethical committee of Ulm University that suggest limited monetary compensation for adolescent study participants. Furthermore adolescents received reward in form of vouchers instead of bank transfers. Otherwise all technical parameters of the functional challenge were the same as in our previous studies. After an expectation period, subjects had to correctly react with a button press to one of two different symbols. In reacting correctly they preserved themselves the previously announced chance to win one Euro. Feedback (outcome) followed the targets disappearance and notified subjects about the amount of money (1€ – win trial or 0€ – lose trial) they won in the trial.

2.6. fMRI acquisition

A 3.0T MR scanner (Siemens MAGNETOM Allegra, Erlangen, Germany) was used to perform T1 anatomical imaging (1 x 1 x 1 mm³ voxels) and fMRI similar to previous experiments. Functional time series were recorded using a T2*-sensitive gradient echo sequence measuring changes in BOLD-contrast. As in our previous studies with adults on the Allegra (Abler et al., 2006, 2007, 2009), we used slightly shortened echo time (TE), reduced slice thickness, and a tilt steeper than the usual AC–PC orientation to minimize the risk of signal loss or distortions in these brain regions. 23 transversal slices were acquired with an image size of 64 × 64 pixels. Slice thickness was 3 mm with 0.75 mm gap resulting in voxel sizes of 3 × 3 × 3.75 mm³. Images were centered on basal structures of the brain including subcortical regions of interest (limbic structures and prefrontal regions). 401 volumes were obtained during each session at a repetition time (TR) of 1500 ms and echo time (TE) of 35 ms.

2.7. fMRI analysis

Image processing and statistical analysis were carried out using Statistical Parametric Mapping (SPM 8, Wellcome Trust Centre for Neuroimaging, London, UK). Preprocessing of individual functional time series included slice timing, realignment to correct for motion artifacts, spatial normalization via the segmentation toolbox into standard MNI space, and smoothing with an 8 mm FWHM Gaussian kernel. Intrinsic autocorrelations were accounted for by first-order autocorrelation modeling and low frequency drifts were removed via high pass filtering.

For individual first level analysis, we defined five regressors for the five different types of reward expectation (exp., 0%, 25%, 50%, 75%, 100%) and eight regressors for the outcome phases depending on reward expectation (0–100%) and actual outcome (win/loss) at different probabilities (Abler et al., 2009). According to their actual durations, trials were modeled as timedly extended events and convolved with the hemodynamic response function. The six realignment parameters modeling residual motion were also added to the individual models.

2.8. Region of interest (ROI) definition

For ROI definition we used anatomical ROIs and peak voxel coordinates from two prior studies on adolescent depression with characteristic results. For the sgACC the MNI-coordinates x/y/z = ±5/25/-10 (Davey et al., 2012) and for the hippocampus the coordinates x/y/z = -18/-12/-16 (van Eijndhoven et al., 2013), were used as starting points. We then defined spheres around these maxima with radius r=6 mm for the left sgACC ROI and r=10 mm for the left hippocampus ROI. The resulting ROIs were then mirrored to the opposite hemisphere to obtain the right sgACC ROI and the right hippocampus ROI. The amygdala ROIs were defined using the standard masks provided by the WFU Pick Atlas for SPM (http://fmri.wfubmc.edu/software/PickAtlas), and the nucleus accumbens ROIs were defined using the masks provided by the Harvard-Oxford cortical and subcortical structural atlases (www.cma.mgh.harvard.edu/fsl_atlas.html).

The estimated mean fMRI signal averaged across all voxels of each ROI in each subject was then extracted separately for win and loss outcomes and the differential activation signal of win minus loss trials was computed. Afterwards, pre-to-post-differences within each group (PAT-W and PAT-I complete) were tested against zero to assess significance on changes over time. As what would be denoted as primary outcome in classic pharmacological treatment studies, relationships between individual fMRI pre-to-post-signal changes and pre-to-post as well as pre-to-follow-up symptom score changes were tested on significance by computing correlation coefficients for the sgACC ROIs in the PAT-I complete sample with 18 participants. Furthermore, to infer significance of treatment effects, directed two-sample t-tests were computed testing on significant interactions of group (PAT-W/PAT-I) and time (pre-/post-) in areas with significant win/lose differences. Since greater effects were expected a priori in PAT-I then PAT-W, we tested unidirectionally.

In the sense of a secondary outcome, fMRI signals from the pretest sgACC ROIs of PAT-I complete were correlated with the pre-to-follow-up changes in symptom scores to assess the predictive value of the imaging results.

3. Results

3.1. Clinical assessments

Within group analyses revealed significant pre-to-post-reductions in the CDRS-R (t(17) = −3.65, p = 0.001) and BDI-II (t(17) = −3.25, p = 0.003) for PAT-I complete (N=18). These symptom improvements remained stable from pre-to-follow-up assessed by means of CDRS-R (t(17) = −3.91, p < 0.001) and BDI-II (t(17) = −4.35, p < 0.001), however with no further significant improvements between post and follow-up in CDRS-R (t(17) = −0.78, p = 0.57) and BDI-II (t(17) = −1.67, p = 0.11). Pre-to-post-changes within PAT-W were not significant (see Table 2). Two-sample t-tests, to assess interaction effects between group (PAT-W/PAT-I) and time (pre/post), were significant for both rating scales, BDI-II and CDRS-R, indicating significant treatment effects of the intervention against waiting (see Table 2).

3.2. fMRI data analysis

A whole brain analyses across all patients prior to waiting or intervention (N=22) was computed to assess pre-test (before intervention or waiting) main effects of the task. Focussing on the outcome phase, we set up a contrast to compare activation between win minus lose trials. The whole brain analysis was thresholded at p < 0.001 at the voxel level, with an extent threshold of 60 contiguous significant voxels per cluster to obtain clusters significant at p < 0.05, family-wise corrected for multiple comparisons. We observed reliable activation within the ventral striatum, amygdala, hippocampus and sgACC (see Fig. 2) as well as in regions of the reward system i.e. pregenual cingulate cortex and lateral prefrontal cortex, additionally.

Results of pre-to-post-differences of averaged signals per each ROI in PAT-I complete showed significant pre-to-post-signal reductions in the bilateral amygdala, bilateral hippocampus and
Table 2
p-Values from significance tests for pre-to-post-symptom improvement and pre-to-post-changes in neural signals in the amygdala, hippocampus and sgACC within and between PAT-I and PAT-W.

<table>
<thead>
<tr>
<th>Diagnostic instruments</th>
<th>Within PAT-I</th>
<th>Within PAT-W</th>
<th>Between PAT-I subgroup</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>complete</td>
<td>(N=18)</td>
<td>PAT-W (N=10) and PAT-W (N=12)</td>
</tr>
<tr>
<td>BDI-II</td>
<td>0.003</td>
<td>0.116</td>
<td>0.042</td>
</tr>
<tr>
<td>CDRS-R</td>
<td>0.001</td>
<td>0.102</td>
<td>0.027</td>
</tr>
<tr>
<td>Regions of interest</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amygdala</td>
<td>L 0.003</td>
<td>0.128</td>
<td>0.010</td>
</tr>
<tr>
<td></td>
<td>R 0.031</td>
<td>0.412</td>
<td>0.192</td>
</tr>
<tr>
<td>Hippocampus</td>
<td>L 0.004</td>
<td>0.396</td>
<td>0.042</td>
</tr>
<tr>
<td></td>
<td>R 0.022</td>
<td>0.335</td>
<td>0.103</td>
</tr>
<tr>
<td>Subgenual</td>
<td>L 0.002</td>
<td>0.451</td>
<td>0.078</td>
</tr>
<tr>
<td>anterior</td>
<td>R 0.005</td>
<td>0.297</td>
<td>0.032</td>
</tr>
<tr>
<td>cingulate cortex (sgACC)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

As eight of the patients in PAT-I complete, participated in the waiting time before being admitted to the intervention, interaction effects were calculated on the remaining subjects of PAT-I and PAT-W. BDI-II= Beck Depression Inventory Revision; CDRS-R = Children’s Depression Rating Scale Revised; L = left brain hemisphere; R = right brain hemisphere; within-group analyses were computed by means of one-sample t-tests and between-group analyses by means of two-sample t-tests.

Bilateral sgACC. By contrast, pre-to-post-signal changes in these brain areas were not significantly different from zero in the PAT-W group (see Table 2; Fig. 3). Pre-to-post-signal change in the ventral striatum was neither significant in PAT-I complete nor the PAT-W group.

For PAT-I, results of pre-to-post-signal differences per each ROI are also summarized in Table 2 as are between-group interaction effects with PAT-W (see also Fig. 3). PAT-I showed significant pre-to-post-signal reductions in the left amygdala $p=0.02$, left hippocampus $p=0.01$ and right sgACC $p=0.02$. Significant interaction effects of group (PAT-I/PAT-W) and time (pre/post), with respect to significant win/loss differences, were observed in the left amygdala, left hippocampus and right sgACC.

3.3. Association between fMRI signal changes in the sgACC and symptom reduction

Following previous findings (Siegle et al., 2006), we correlated pre-to-post-intervention BOLD signal changes in the sgACC of PAT-I complete (N=18) with symptom improvement in pre-to-post and pre-to-follow-up clinical assessments of the BDI-II and CDRS-R scales. For the BDI-II, pre-to-post-difference scores were significantly correlated with pre-to-post-signal changes in the left ($r=0.57, p=0.01$) and right ($r=0.54, p=0.02$) sgACC. Correlation coefficients further increased with pre-to-follow-up difference scores for the BDI-II (left sgACC: $r=0.69, p=0.002$; right sgACC: $r=0.73, p=0.001$; see Fig. 4 left graph). No significant correlations were observed for the CDRS-R in either sgACC region with pre-to-follow-up difference scores.

3.4. Association between pre-treatment sgACC activity and symptom reduction

Furthermore, pre-treatment sgACC activation was correlated with pre-to-follow-up symptom changes in the BDI-II (left sgACC: $r=-0.56, p=0.02$, right sgACC: $r=-0.59, p=0.01$, see Fig. 4 right graph) with altered brain activation before the intervention predicting clinical improvement. For the CDRS-R, pre-to-follow-up symptom improvement again could not be predicted by pre-treatment activation in the sgACC.

4. Discussion

Significant clinical and neural effects of a five weeks cognitive behavioral group therapy could be demonstrated in adolescents with major depressive disorder. In line with common models of depression (Davidson et al., 2002), activations of brain regions previously related to treatment effects, mainly in adults and with pharmacotherapy, changed significantly with successful psychotherapeutic treatment in adolescents as well. Primarily, improvement in depressive symptoms was correlated with changes in sgACC activation. In a second line of analysis, individual expressions of pre-treatment activations of the sgACC could be demonstrated to predict individual therapeutic response. Additional analyses confirmed the effects relative to a waiting condition.

Our results of modulated activity of the amygdala, hippocampus and sgACC after successful CBT-G can be interpreted in the light of the model of Phillips et al. (2003), who identified two relevant neural systems for perception and regulation of emotions: the dorsal system, including the hippocampus, which is important for the top-down regulation of emotions, and the ventral system, including the amygdala and the sgACC which are important for the identification of emotional stimuli and bottom-up modulation of affective states. Our present result of altered responsiveness of the amygdala and sgACC after CBT can therefore be interpreted that CBT may help with changing activity of brain regions that mediate bottom-up production of affect. Particularly sgACC activity has been reported to play a significant role in dysfunctional processing of negative stimuli (Disner et al., 2011), negative bias for self-evaluation, and impaired feedback of positive stimuli (Murray et al., 2011). Modified amygdala and hippocampus activation was demonstrated to relate to ruminative thoughts and biased memory for negative stimuli respectively (Disner et al., 2011), and to mediate emotional memory that has been shown to be impaired in depression (Tahmasian et al., 2013). As the hippocampus is a
The region where cognitive processes are integrated with and can be biased by emotional input, it has been suggested to contribute to executive functions including effortful regulation of affective states (Phillips et al., 2003) which in turn may be particularly sensitive to cognitive interventions. Changing hippocampal activation by psychotherapy may reflect a change in its ability to modulate top-down processing and facilitating integration of previous experiences for emotion regulation.

Previous studies have demonstrated fMRI activation of amygdala, hippocampus and sgACC to be modulated by antidepressants.
in depressed patients (Arnone et al., 2012, Godlewksa et al., 2012, Sheline et al., 2001). However, antidepressants in healthy subjects have been associated with similar effects (Abler et al., 2011, Macoveau, 2014), which shows that changes in brain activation upon antidepressant treatment are ambiguous with respect to the underlying factors (symptom, improvement and/or medication). In line with one of the few studies on neural effects of psychotherapy, although in adults (Fu et al., 2008), in the present study we show that activity of the amygdala, sgACC and hippocampus changed in alignment with symptom improvement upon clinically successful psychotherapy. As our subjects were naïve to pharmacological treatment, present results therefore support the notion that neural activity changes most likely relate to treatment success rather than to pharmacological treatment. Here, our findings may close a gap. Also consistent with previous studies is our finding of a strong correlation between symptom improvement and activity in the sgACC, which was also reported by Fu et al. (2008) and Siegle et al. (2006, 2012) for adult samples, Fu et al. (2008) found a significant relationship with linear load–response activity in the dorsal anterior cingulate region in patients who showed greater improvement with CBT. Siegle et al. (2006) reported a significant association between reduced pretreatment activity in the sgACC and subsequent treatment response. In our study relatively increased pretreatment activity in the sgACC was associated with subsequent treatment response. While Siegle et al. (2006) focused on activation related to negative emotional stimuli, we investigated activation related to positive (win) versus negative (loss) stimuli.

In contrast to Yang et al. (2009) and Fu et al. (2008), who demonstrated associations between signal change and treatment response as assessed by means of clinical interviews, we found that the self-report scales were better predictors of clinical changes. Similar to the results reported by Siegle et al. (2006) our findings support the assumption that subjective impression may better reflect changes in brain activation than outer appearance assessed by external observation.

To our knowledge the present study is the first that investigated neural effects of psychotherapy in adolescents in a waitlist control design. Allowing eight participants from the waiting list condition to participate in the intervention after waiting, was done for ethical reasons and adaptive to clinical circumstances but not ideal with respect to scientific standards. Future studies should take this issue into account by enrolling larger sample sizes as was actually possible. This would also overcome the present limitation of a skewed gender recruitment, limiting generalizability to male patients. Besides that, future studies should try to evaluate the ideal dose of CBT by investigating programs with greater or smaller session numbers and, additional follow-up fMRI measurements up to six to twelve months after termination of psychotherapy to investigate long-term effects. As functional connectivity was shown to predict whether a subject was clinically depressed or healthy (Craddock et al., 2009), future studies should also consider to investigate functional connectivity and changes thereof as potential biomarkers of putative treatment effects.

We demonstrate a distinct neural signature of successful group psychotherapy in adolescents with depression compared to adolescents who waited with minimal treatment. Activation of the amygdala, hippocampus and sgACC, commonly reported as relevant in depression (Arnone et al., 2012, Fu et al., 2007, 2008, Godlewksa et al., 2012, Gotlib et al., 2005, Kumari et al., 2003, Rosenblau et al., 2012, Sheline et al., 2001, Yang et al., 2010), changed with amelioration of depressive symptoms. Our study supports models suggesting that dysfunctional neural mechanisms of emotion regulation in depression can be reached by psychotherapy, at least in the early stages of the illness and may therefore constitute a state rather than a trait marker. As chronic courses of depression clearly have shown to modulate neural activity in the long run and to leave neural scars even in remission (Elliott et al., 2012), this emphasizes the potential impact of interventions early in the course of the illness as possible. Our finding of rather strong correlations between individual expressions of brain activation predicting individual therapeutic response may inspire further research on individualized therapies.

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Conflict of interest

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