



Case-control study of the low intensive autism-specific early behavioral intervention A-FFIP: Outcome after one year

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Abstracts: *Objective:* In current international research, early intervention in children with autism-spectrum disorder (ASD) focuses on naturalistic developmental behavioral interventions (NDBI). The manualized Frankfurt Early Intervention Program for preschool-aged children with ASD (A-FFIP) implements NDBI principles within a low-intensity approach of 2 h intervention/week. The present case-control study established effect sizes of change in autistic symptoms, comorbid behavioral problems as well as IQ after one year. *Methodology:* An intervention group ($N = 20$; age: 3.4–7.9 years) and a treatment-as-usual control group ($N = 20$; age: 3.2–7.3 years) of children with ASD were matched for developmental and chronological age. The outcome measures used were the ADOS severity score, the Child Behavior Checklist, and cognitive development. *Results:* After one year, the A-FFIP group showed a trend towards greater improvement in autistic symptoms ($\eta^2 = .087$ [95%-CI: .000–.159]) and significantly greater improvements in cognitive development ($\eta^2 = .206$ [CI: .012–.252]) and global psychopathology ($\eta^2 = .144$ [CI: .001–.205]) compared to the control group. *Conclusion:* The efficacy of A-FFIP should be established in a larger, sufficiently powered, randomized controlled study.

Keywords: ASD, autism, early intervention, NDBI, A-FFIP

Autismus-spezifische, verhaltenstherapeutische Frühintervention (A-FFIP): Ergebnisse einer Fall-Kontroll-Studie nach einem Jahr

Zusammenfassung: *Fragestellung:* Frühförderansätze für Kinder mit Autismus-Spektrum-Störung (ASS), die entwicklungsorientiert vorgehen und verhaltenstherapeutische Techniken in der natürlichen Lernumgebung des Kindes einsetzen, stehen aktuell im Zentrum internationaler Forschung. Das manualisierte Frankfurter Frühinterventionsprogramm für Vorschulkinder mit ASS (A-FFIP) arbeitet mit diesen Grundsätzen im Rahmen einer niederfrequenten Förderung von 2 Stunden/Woche. In der vorliegenden Fall-Kontroll-Studie werden Effektgrößen bezüglich der Entwicklung der autistischen Symptomatik, komorbider Verhaltensprobleme sowie IQ nach 1-jähriger A-FFIP Förderdauer im Vergleich zur Standardbehandlung beschrieben. *Methodik:* Therapie- ($N = 20$; Alter 3.4–7.9 Jahre) und Kontrollgruppe ($N = 20$; Alter 3.2–7.3 Jahre), die die ortsübliche Intervention erhielt, waren zu Beginn der Intervention bezüglich Entwicklungsalter und Alter gematcht. Untersuchte Zielgrößen waren der ADOS-Schweregradindex, die Child Behavior Checklist und die kognitive Entwicklung. *Ergebnisse:* Nach 1-jähriger Förderung zeigte die A-FFIP-Gruppe einen Trend zu einer stärkeren Verbesserung der autistischen Symptomatik ($\eta^2 = .087$ [CI: .000–.159]), sowie eine stärkere Verbesserung der kognitiven Entwicklung ($\eta^2 = .206$ [CI: .012–.252]) und globalen Psychopathologie ($\eta^2 = .144$ [CI: .001–.205]) als die Kontrollgruppe mit jeweils mittleren bis hohen Effektgrößen. *Schlussfolgerung:* A-FFIP sollte bezüglich seiner Effektivität in einer größeren randomisiert-kontrollierten Studie mit ausreichender Teststärke untersucht werden.

Schlüsselwörter: ASS, Autismus, Frühförderung, NDBI, A-FFIP

Introduction

Rising prevalence rates of autism spectrum disorder (ASD) have led to a growing number of intervention programs (Elsabbagh et al., 2012). Several early-intervention programs for toddlers and preschool-aged children with ASD

have been developed and studied predominantly in the US and the UK (Murza et al., 2016; Oono et al., 2013; Reichow et al., 2012; Weitlauf et al., 2014). Early intervention programs differ greatly regarding the underlying theoretical concept (behavioral, discrete trial, naturalistic, developmental, or combined), use of evidence-based methods, set-

ting (home, center-based), intensity (weekly treatment hours, duration), and the degree of therapist and parental involvement (therapist-delivered, therapist-supported, parent-delivered, parent-supported, or a combination thereof).

So-called naturalistic developmental behavioral interventions (NDBI) represent the current state of the art (Schreibman et al., 2015). NDBIs are implemented in natural settings, involve shared control between child and therapist, utilize natural contingencies, and use a variety of behavioral strategies to teach developmentally appropriate and prerequisite skills. NDBIs can be differentiated in comprehensive (such as the Early Start Denver Model, ESDM; Rogers & Dawson 2010) and target-focused programs (such as the Preschool Autism Communication Trial, PACT; Green et al., 2010).

Targeted programs are designed to address the core symptoms of autism by teaching specific, early, nonverbal social communication and learning skills, which are impaired in children with ASD. This includes social reciprocity, joint attention, and imitation. The intensity of these programs is generally low. Some of these programs also address parent-child interactions and are provided as parent-delivered programs. Improvements have been shown for parent-child interaction (Green et al., 2010), language outcome (Kasari et al., 2012), and autism core deficits (Pickles et al., 2016).

Comprehensive programs in turn address developmental areas and outcomes, and therefore are often designed to be applied at a higher intensity, between 25 to 40 hours per week (Reichow et al., 2012). Positive treatment outcomes have been found mainly for IQ, adaptive behavior, and language development, whereas improvement of autism-specific symptoms has rarely been reported for intensive NDBI programs of high methodological quality (Dawson et al., 2010; Reichow, 2012; Warren et al., 2011). Highly intensive programs are expensive and are available for only a small number of children and their families. Several authors have emphasized the need for comprehensive but low-intensive programs that can be implemented in community settings and provided through public social and health services (Colombi et al., 2018; Dawson & Bernier, 2013; Kaale et al., 2014; Vismara et al., 2009).

Recently, the comprehensive ESDM program, originally conceptualized and evaluated with high weekly intensity (15 h/week therapist-delivered and additional 16 h/week parent-delivered; Dawson et al., 2010) was applied in different community settings at a far lower intensity (3–6 h/week; therapist-delivered). These first low-intensity studies with a comprehensive NDBI approach showed promising results regarding gains in cognitive and adaptive skills (Colombi et al., 2018; Devescovi et al., 2016), comparable to more intensive approaches. Yet improvement of core autism symptoms failed to appear. Additional research focusing on improving

autistic symptoms via low-intensity comprehensive programs is thus needed to ultimately increase the availability of evidence-based, autism-specific interventions through the public healthcare system for all children with ASD.

Germany provides approximately 2–5 hours per week of early intervention via public social and healthcare services. Unfortunately, most currently available interventions are not autism-specific, and only 35 % of the children with ASD actually receive behavioral or developmentally based early intervention (Salomone et al., 2015). To improve the standard of care, we developed a comprehensive NDBI, namely, the Frankfurt Early Intervention Program (A-FFIP; Teufel et al., 2017), which corresponds to the needs of the German welfare system (Weinmann et al., 2009).

The A-FFIP is manualized as a comprehensive, low-intensity program (2 h/week over 2–3 years) and contains the above-mentioned evidence-based elements and methods, thus qualifying it as NDBI (Schreibman et al., 2015). More information about the program contents and tasks is provided in the Supplementary Material Section.

Using A-FFIP, a small one-year pre-post study (Freitag et al., 2012; Kitzerow et al., 2014; Kitzerow et al., 2016) observed medium-to-large improvements in language and cognitive abilities as well as adaptive behavior and autism-specific symptoms. A strong limitation of these first publications, however, was the lack of a control group. The current study describes the effects of one-year intervention by A-FFIP compared to a treatment-as-usual clinical control group on autistic symptoms, comorbid psychopathology, and cognitive development in preschool-aged children with ASD.

Methods

Study Design

Group enrolment was based on waiting-list contingencies and place of residence. All families who lived in the residential area were offered a waiting-list placement for A-FFIP after ASD diagnosis. A-FFIP intervention was offered according to the position on the waiting list, and all children were successively included into the intervention group. All preschool-aged children who received A-FFIP at the Autism Research and Intervention Center of Excellence in Frankfurt during the study were enrolled if parents were willing to participate in the study. The baseline assessment (T1) was done within 6 weeks prior to the start of the intervention, and the follow-up assessments (T2) took place after one year ($M = 12.7$ month; $SD = 1.0$).

Children of families who lived too far away, who had to wait longer than 12 months for A-FFIP, or who chose to do

another intervention were offered participation in the control group.

Children were included once all baseline assessments had been conducted within 3 months after diagnosis, when the families did not receive A-FFIP within the following 12 months, and when the families participated in the follow-up assessments (T2), which took place after one year ($M = 12.7$ month; $SD = 1.9$).

All assessments were done by researchers not involved in the child's therapy. The allocation of the intervention was independent of study participation. The study design was approved by the local Ethics Committee of the Medical Faculty at JW Goethe University Frankfurt. All parents gave written informed consent to participate with their child in the study.

Participant Characteristics

The study group consisted of 38 male and 2 female children (5%; both in the A-FFIP group) with ASD diagnosed according to ICD-10 criteria by an experienced clinician, based on the information by the parents in the Autism Diagnostic Interview-revised (ADI-R; Bölte et al., 2006) and direct observation by the Autism Diagnostic Observation Schedule (ADOS; Rühl et al., 2004). The A-FFIP group comprised 15 children (75%) diagnosed with autism, 2 (10%) with atypical autism, and 3 (15%) showed Asperger syndrome according to ICD-10 criteria. The TAU group had 12 children (60%) diagnosed with autism, 2 (10%) with atypical autism, and 6 children (30%) showed Asperger syndrome according to ICD-10 criteria.

Children with a developmental or intelligence quotient (EQ/IQ) < 35 or with a mental age < 18 months were excluded from the study. Other exclusion criteria were severe sensory impairments, cerebral palsy, epileptic seizures un-

treable by antiepileptic therapy, other chronic neurological and motor disorders, severe psychosocial deprivation, insufficient care by parents, attachment disorder, and institutional upbringing.

At baseline, the groups did not differ regarding autism symptom severity, chronological or developmental age, or for any other outcome measure. More details are shown in Table 1.

In the A-FFIP group, 4 children received psychotropic medication during the course of the study (Abilify, risperidone). To exclude confounding by medication, we did additional sensitivity analyses on the group without psychotropic medication only. At baseline all children went to kindergarten, and some children received part-time individual support not specialized in ASD.

Intervention

The Frankfurt Early Intervention Program (A-FFIP) is an individualized developmental behavioral and naturalistic approach with low intervention frequency (2 h/week) and intensive parental and kindergarten involvement (Teufel et al., 2017). Children included in the current study received a mean of 1.1 h/week ($SD = 0.3$) A-FFIP in an outpatient setting over 12 months (total hours mean = 57.9 h/year; $SD = 16.1$). Because of holidays, illness, and other individual factors, the actual intervention intensity was lower than the planned maximum intensity (like comparable interventions, e.g., ESDM, Dawson et al., 2010). More detailed baseline data are provided in Table 1.

Children in the control group received treatment as usual representative of a German sample (Salomone et al., 2015). Thereof, 10 children (50%) received an ASD-specific intervention with varying intensity from 0.5 to 10 h/

Table 1. Baseline sample characteristics for the intervention and control group.

	A-FFIP (N = 20)			TAU (N = 20)			p
	Mean	SD	Range	Mean	SD	Range	
Age at study entry	5.5	1.5	3.4–7.9	5.0	1.2	3.2–7.3	.350
Developmental age	4.1	1.9	1.6–8.2	4.2	1.8	1.6–8.2	.715
Developmental quotient	71.7	25.2	37.3–115	81.6	23.7	47.5–134	.213
ADOS severity score	7.3	1.4	5–10	6.5	1.8	4–10	.118
Autism-specific weekly intervention hours	1.1	0.3	0.6–1.7	2.1	2.8	0.5–10	.740
Additional weekly therapy hours*	0.9	0.9	0–3	1.5	0.9	0–3	.029

Note. ADOS: Autism Diagnostic Observation Schedule; A-FFIP: Frankfurt Early Intervention Program; TAU: treatment as usual; *such as general (not ASD-specific) early intervention, occupational therapy, speech, and language therapy.

week ($M = 2.1$; $SD = 2.8$). These interventions were based on applied behavior analyses (ABA) approaches (30%), TEACCH- (30%), social skills training (10%), or undefined (30%).

Instruments

The Autism Diagnostic Interview-Revised (ADI-R; Bölte et al., 2006; Lord et al., 1994) is a semistructured parent interview that assesses autism symptoms across three domains: social relatedness, communication, and repetitive, restricted behaviors. Together with the Autism Diagnostic Observation Schedule (ADOS; Lord et al. 1999; Rühl et al., 2004) it is considered the gold standard of autism diagnosis (Falkmer et al., 2013).

The ADOS is a semistructured standardized observation that measures autism symptoms in social relatedness, communication, play, and repetitive behaviors. Here, we used modules 1 to 3, depending on the respective child's language development. The ADOS severity score (Gotham et al., 2009) was calculated to achieve comparability across the different modules. Double coding of 11 ADOS videos (14.1%) showed satisfying interrater reliabilities. The intraclass correlations (ICC) of the ADOS algorithm domain scores were all comparable to the interrater reliabilities from the original German ADOS norming study (Rühl et al., 2004): Communication ICC = .86; Socialization ICC = .91; Stereotyped behavior ICC = .81. The interrater reliability of the ADOS severity score showed an ICC = .89.

The Social Responsiveness Scale (SRS; Bölte & Poustka 2008) is a 65-item parent rating scale (coded on a 4-point Likert scale) on social responsiveness over the previous 6 months.

The Social Communication Questionnaire (SCQ; Bölte & Poustka 2006) is a 40-item parent-report screening questionnaire (with *yes/no* coding) for autism based on the ADI-R. Here, we implemented the "current behavior" version.

Developmental age (DA) was assessed either by the cognitive scale of the Bayley Scales II (Bayley-II; Reuner et al., 2008) in children with a mental age below 30 months; or by the Snijders-Oomen Nonverbal Intelligence Test 2½-7 (SON-R; Tellegen et al., 2007). A developmental quotient (DQ) from the Bayley-II was calculated as follows: $DQ = DA/CA \times 100$.

The parent rating form of the Vineland Adaptive Behavior Scales II (VABS-II; Sparrow et al., 2005) is a standardized adaptive behavior questionnaire that assesses the child's development of personal independence and social responsibility by gathering information about day-to-day activities. American norms were used to calculate the level of adaptive functioning.

The Aberrant Behavior Checklist (ABC; Aman et al. 1985) is a 58-item parent questionnaire on problematic behavior in children with disabilities.

Psychiatric symptoms in different domains were assessed with the German version of the Child Behavior Checklist (CBCL 1½-5; Achenbach 2002; CBCL 4-18; Achenbach 1998). The CBCL is a widely used parent report assessing global psychopathology and behavioral problems (Berubé, 2010). Here, we compared the total *T*-score and the second-order *T*-scores assessing internalizing and externalizing psychopathology.

Statistics

We calculated the interrater reliability of the ADOS severity score using intraclass correlation coefficients from the SPSS model for one-way random single measures (IBM Statistics 22). All other statistical analyses described below were conducted by SAS version 9.4 (SAS Institute Cary, NC, USA). Baseline differences between groups were compared by the Wilcoxon rank-sum test (two-sided). The diagnostic categories between groups were compared by χ^2 -test. Group \times Time interaction effects were calculated by repeated measures analyses of variance (ANOVA with repeated measures). *F*-test statistic, *p*-value, partial η^2 , and its 95% confidence intervals are reported in the text. Additional results and parameters are provided in the supplementary materials. Missing data were not replaced. No correction for multiple testing was done as the current study aimed at describing effect sizes in an exploratory way. *p*-values and 95%-confidence intervals of effect sizes are reported descriptively.

Results

Figures 1, 2, and 3 show the results of ADOS, IQ, and CBCL development of both groups over time. Table A in the supplementary material displays the complete data of the one-year outcome, by group, within-group change scores relative to baseline, and the group comparisons for all relevant measures.

Autism-Specific Development

A trend for a Group \times Time interaction with a medium effect size was found for the ADOS severity score ($F = 3.44$; $p = .072$; $\eta^2 = .087$ [CI: .000-.159], for the group without medication (nonmed group): $F = 5.29$; $p = .028$; $\eta^2 = .142$ [CI: .000-.211]). The A-FFIP group lost $M = -1.3$ points ($SD = 1.6$), the TAU group $M = -0.2$ ($SD = 2.0$).

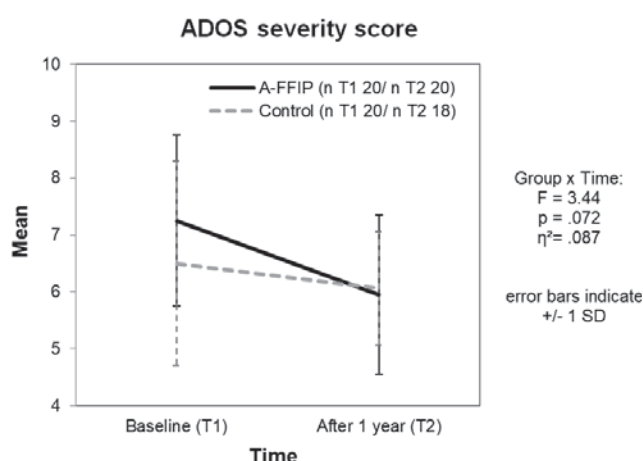


Figure 1. Development of the ADOS severity score for the intervention and the control group after one year.

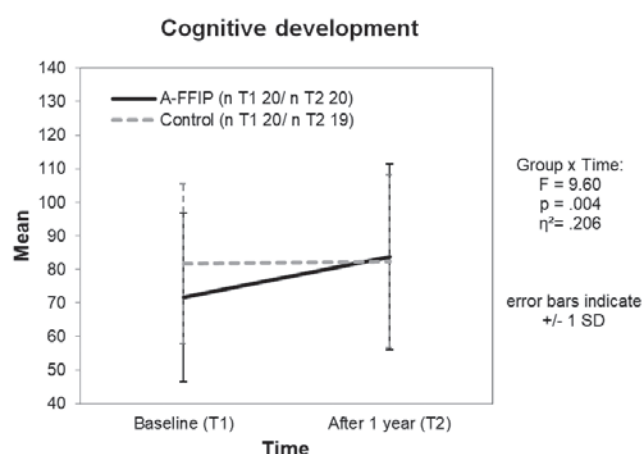


Figure 2. Cognitive development for the intervention and the control group after one year. Developmental or intelligence quotient was assessed with the Bayley scales-II or with the SON-R 2 ½–7.

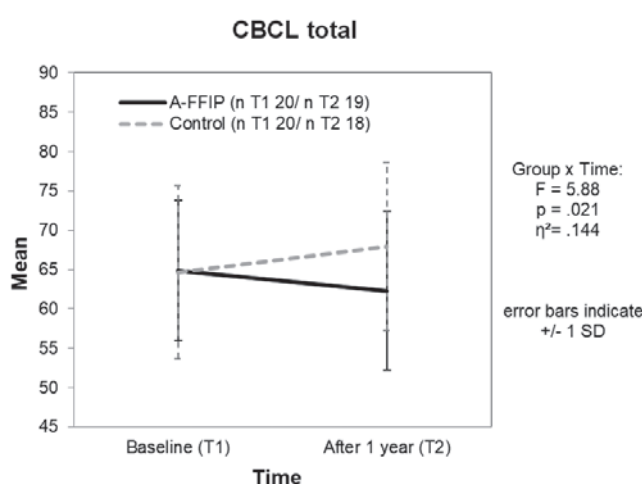


Figure 3. Development of the Child Behavior Checklist (CBCL, parent rating) total *t*-scores for the intervention and the control group after one year.

Parents similarly described a trend for change in the SRS social motivation subscale with a medium effect size (Group \times Time $F = 3.10$; $p = .087$; $\eta^2 = .081$ [CI: .000–.154]; for the nonmed group: $F = 1.99$; $p = .168$; $\eta^2 = .059$ [CI: .000–.141]). The A-FFIP group lost $M = -8.9$ points ($SD = 11.6$), TAU lost $M = -1.95$ ($SD = 12.6$).

The subscale social interaction of the SCQ parent questionnaire also showed a trend for a Group \times Time interaction with a medium effect size ($F = 3.49$; $p = .071$; $\eta^2 = .096$ [CI: .000–.166]; for the nonmed group: $F = 2.47$; $p = .126$; $\eta^2 = .076$ [CI: .000–.157]). The A-FFIP group lost $M = -1.6$ points ($SD = 3.6$), whereas the mean of the TAU group increased slightly ($M = 0.4$; $SD = 2.7$).

Adaptive Functioning

A trend for a Group \times Time interaction with a medium effect size was found for adaptive behavior in the subscale daily living ($F = 2.87$; $p = .099$; $\eta^2 = .072$ [CI: .000–.148]; for the nonmed group: $F = 2.33$; $p = .137$; $\eta^2 = .066$ [CI: .000–.149]). The A-FFIP group gained $M = 3.2$ points ($SD = 9.8$), while TAU lost $M = -4.1$ points ($SD = 16.2$).

Cognitive Development

A significant Group \times Time interaction was observed for the developmental quotient with a high effect size in favor of the A-FFIP group ($F = 9.6$; $p = .004$; $\eta^2 = .206$ [CI: .012–.252]; for the nonmed group: $F = 8.25$; $p = .007$; $\eta^2 = .200$ [CI: .008–.255]). Children in the A-FFIP group gained on average 12.1 points ($SD = 10.7$) in age-standardized cognitive development, while children in the TAU group gained $M = 1.5$ points ($SD = 10.6$).

Additional Psychopathology

No Group \times Time interaction was found for any parent-rated ABC subscales. A significant Group \times Time interaction with a high effect size was observed regarding the parent-rated CBCL total score ($F = 5.88$; $p = .020$; $\eta^2 = .144$ [CI: .001–.205]; for the nonmed group: $F = 5.21$; $p = .029$; $\eta^2 = .144$ [CI: .000–.212]). The A-FFIP group lost $M = -2.7$ points ($SD = 6.3$) on the total score, while children in the TAU group showed increased psychopathology compared to baseline ($M = 3.6$; $SD = 9.2$).

On the internalizing subscale, which comprises many ASD-specific behaviors like anxiousness, being withdrawn, and social problems, a trend for a Group \times Time interaction with a medium effect size was found ($F = 3.02$; $p = .091$; $\eta^2 = .079$ [CI: .000–.153]; for the nonmed group:

$F = 1.81$; $p = .188$; $\eta^2 = .055$ [CI: .000–.138]). The A-FFIP group lost $M = -3.6$ points ($SD = 5.1$), while TAU lost $M = -0.6$ ($SD = 5.4$).

Discussion

A-FFIP was developed as a comprehensive, individualized and cost-effective low intensity NDBI based on the empirical findings of different naturalistic and developmentally based learning approaches (Schreibman et al., 2015). Most early intervention programs with an NDBI approach are either comprehensive with a high intensity (such as ESDM; Dawson et al., 2010) or targeted with a low intensity (such as PACT; Green et al., 2010). A-FFIP is one of the first programs to be conceptualized and manualized as both comprehensive (by addressing five developmental domains and six basic core abilities) and low intensive (intensity of 2 hours per week center-based intervention). Here, we report for the first time the one-year effect sizes based on a clinical trial with a matched, but not randomized control group.

Medium effects, albeit not reaching significance, were achieved regarding different measures of autism symptom severity by A-FFIP compared to TAU. The absolute change of the ADOS severity score in the A-FFIP group is comparable to the change induced by the targeted low-intensity (weekly sessions over 6 months, followed by monthly sessions over 6 months) parent-mediated (20–30 min daily practice) PACT trial with children of the same age (Pickles et al., 2016). Children in the PACT treatment group also lost a mean of 1.3 points ($SD =$ not available [NA]) in the ADOS severity score after one year of parent-child interaction and communication training. For the comprehensive ESDM approach with younger children implementing high intensity (15 h/week therapist-delivered and 16 h/week parent-delivered), also only a trend for a Group \times Time interaction (no effect size reported) regarding the ADOS severity score was reported in favor for the intervention group, which lost a mean of 0.7 points ($SD = NA$), while the value of the control group increased by a mean of 0.4 points ($SD = NA$) after one year (Dawson et al., 2010). When the ESDM approach was applied within a low-intensity setting (3 h/week) with younger children, no significant changes were found, and again no effect sizes of the ADOS severity score after 15 months were reported (Devescovi et al., 2016). Most other NDBIs assessed the change of autism-related variables such as joint attention, symbolic play, joint engagement, or imitation (Ingersoll et al., 2012; Kaale et al., 2012; Kasari et al., 2006; Kasari et al., 2015) but did not use a global outcome measure like the ADOS. When the ADOS was done in NDBI studies, the

reported outcome was either a change in diagnostic categories (Solomon et al., 2014) or in domain scores (Wetherby et al., 2014), but not in the ADOS severity score. In EIBI studies of higher quality, the ADOS was also not used as an outcome measure (Reichow et al., 2012). Taken together, the effect size as well as the absolute change in autistic symptoms achieved by A-FFIP is comparable to the parent-child interaction training PACT as well as the high-intensity ESDM approach – but did not achieve significance because of the low power and limited sample size of the present study.

In addition, the A-FFIP showed a large effect size on cognitive development with a mean improvement of 12.1 points ($SD = 10.7$) compared to a mean improvement of 1.5 points ($SD = 10.6$) by TAU after one year. Although no significant baseline differences, because of high variance between the groups were found, the TAU group started at a descriptively higher DQ/IQ level, and after one year, no differences between A-FFIP and TAU (mean IQ of both groups in the low average IQ range around 80 [$SD = 25.8$ – 27.7]) were observed. Similar gains in IQ were reported by high-intensity interventions after one to three years (~11–15 points; $SD = NA$; Dawson et al., 2010; Reichow et al., 2012). But in these studies, the investigated groups started with (descriptively) more comparable baseline scores. Thus, for the present study, it remains unclear whether the group differences regarding cognitive development might result from ceiling effects in the control group or selection bias. Therefore, the present IQ results should be interpreted with caution.

Only small, negligible effects were found for change in adaptive behavior after one year. Change in adaptive behavior in previous early intervention studies was also highly variable after one year of intervention, possibly because of different characteristics of the included children regarding age, mental abilities, and adaptive behavior at baseline (Reichow et al., 2012; Warren et al., 2011; Weitlauf et al., 2014), or the psychometric properties of the implemented measures. In the original ESDM study, which included younger children than the present study, the VABS scores decreased on all subscales in both groups, except the communication subscale, and there was no Group \times Time effect after one year, similar to our study (Dawson et al., 2010). In a less intensive ESDM-based approach with slightly younger children than A-FFIP at start of intervention, although the scores of all VABS subscales increased, no significant Group \times Time interaction was found after 6 months (Colombi et al., 2018). Most of the targeted approaches did not study adaptive behavior as outcome.

Interestingly, the A-FFIP group showed a significant decrease with a large effect size of additional parent-rated psychopathology indicated by the CBCL total score. Especially a reduction of internalizing psychopathology

seems to underlie this finding. Other studies on early intervention did not assess psychopathology beyond core ASD symptoms, so that results cannot be compared. It is likely that the same A-FFIP ingredients increasing social motivation may also lead to a reduction of internalizing psychopathology.

A-FFIP as a NDBI contains several natural learning program ingredients, but it does not implement as intensively as ESDM the classical discrete trial methods – and it focuses on a far broader range of developmental areas than the targeted programs. The following A-FFIP characteristics may have led to improvement of core autism symptoms, reduction of internalizing behavior, and cognitive gains: By therapist-delivered intervention, the children showed gains in basic nonverbal and learning skills in a broad range of areas impaired in ASD (attentional control, joint attention, imitation, representation, planning, and self/other distinction). Generalization is supported by including parents in the therapeutic setting, teaching parents how to support the child using the acquired skills at home, and by supporting a positive parent-child interaction. Targeted early intervention studies showed that teaching the core basic abilities included in A-FFIP leads to improvement in exactly these core abilities, for example, joint attention (Murza et al., 2016). Also, an increase in more distant abilities, occurring later in development, and a positive parent-child interaction are achieved by these methods (Kasari et al., 2008, 2012; Pickles et al., 2016; Solomon et al., 2014). For example, a joint attention and play intervention resulted in improved language scores one year later (Kasari et al., 2008, 2012). Similarly, in intervention studies resulting in improvement of the targeted parent-child interaction and communication, distant gains such as improvement of autistic symptoms (Green et al., 2010) or the global functional level (Solomon et al., 2014) were reported. In addition, A-FFIP works with natural reinforcement as well as taking on the child's interests, which likely leads to an increase in social motivation. Thus, core ASD symptoms as well as cognitive abilities may improve because the children themselves become interested in social interaction, play, and other aspects of their environment, which may enable them to acquire new skills independently of the intervention. In addition, the inclusion of parents into the therapist-child training session and the psychoeducation of the parents as well as kindergarten teachers may support the generalization of skills.

Limitations

We observed a high variability in all outcome measures at baseline and after one year, which – despite the observed medium effect sizes – resulted only in trends, but no nomi-

nally significant findings of improvement of ASD symptoms by A-FFIP. A high variability in outcomes has been observed in almost all intervention studies in ASD (Reichow et al., 2012; Weitlauf et al., 2014).

In the intervention group, four children received psychotropic medication. Sensitivity analyses in the nonmedicated sample resulted in comparable effect sizes to the “whole-group-results” regarding ADOS, IQ, CBCL, and ABC, but smaller effect sizes in the parent questionnaires SRS and SCQ. Thus, core behavioral and cognitive changes were overall stable, and confounding by medication can be excluded. Still, further large, well-powered studies should assess the role of medication on intervention outcome by moderator analysis.

In addition, we did not perform randomization for group allocation. Still, both groups were matched regarding chronological and developmental age at start of the study, and the children represent a standard community sample. In order to plan and perform large-scale phase-III efficacy studies of a new intervention, we would need field-tested, nonrandomized and randomized studies with small sample sizes as a necessary first step (Lord et al., 2005; Rogers & Vismara 2008).

A-FFIP was conceptualized as a low-intensity and comprehensive intervention for preschool-aged children with ASD within the German welfare context. The current approach was compared to TAU in Germany, which also is mostly low intensive, but largely not ASD-specific. To examine whether low-intensity approaches such as A-FFIP are comparable to more intensive and ASD-targeted approaches, future studies need to specially focus on this important research question.

In the present study, the ratio of females/males was lower than that reported in epidemiological studies. Because the current study recruitment was naturalistic by waiting-list placement, no children were excluded from treatment because of their characteristics or sex. Gender ratios vary a lot between different intervention studies, and a similar overrepresentation of males has been reported elsewhere (Reichow, 2012; Rogers & Vismara, 2008).

The ADOS was chosen as outcome measure in order to objectively measure autistic symptoms in an observer-blind fashion independent of parents, who are involved into the intervention and thus cannot be blinded. The ADOS, however, was not designed to measure change in autism-specific symptoms over time and thus shows a low sensitivity for change. Using a more appropriate instrument might have led to detecting larger and more subtle changes in autistic symptoms (McConachie et al., 2015). Future studies should take more sensitive instruments into consideration, for example, the BOSCC (Grzadzinski et al., 2016; Kitzerow et al., 2016), which was not available when the current study was being planned.

Conclusion

This exploratory case-control study reports medium to high effect sizes of change in various outcome measures for children in a one-year A-FFIP intervention compared to a nonrandomized TAU control group. A-FFIP is a therapist-mediated, low-intensity (2 h/week), manualized comprehensive program that implements evidence-based developmental and behavioral techniques and involves parents into the intervention. The study emphasizes the important role of NDBI approaches in the early intervention of ASD and fuels the debate on necessary treatment intensity. The program is feasible for children, parents, and therapists, and it has been established within a given care environment for preschool-aged children. A sufficiently powered, randomized controlled trial needs to be done to establish efficacy and to replicate the preliminary findings of the present study.

Electronic Supplementary Material

The electronic supplementary material (ESM) is available with the online version of the article <https://doi.org/10.1024/1422-4917/a000661>.

ESM 1. List.

Detailed description of the Frankfurt early intervention program (A-FFIP).

ESM 2. Table.

One-year outcomes.

ESM 3. Tables.

Full model information of all ANOVAs from the complete sample ($N = 2 \times 20$).

ESM 4. Figures and Tables.

Data and graphics for the nonmedicated subgroup.

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All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

Informed Consent

Informed consent was obtained from all parents of the children included in the study.

Conflicts of Interest

The authors JK and KJ do not report any conflict of interest. The authors KT, CW, and CMF developed the A-FFIP approach and receive royalties for writing the intervention manual. CMF has

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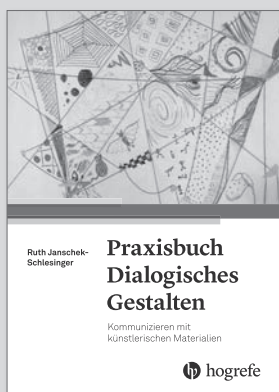
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