Pivotal response treatment for school-aged children and adolescents with autism spectrum disorder: a randomized controlled trial

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Pivotal Response Treatment for School-Aged Children and Adolescents with Autism Spectrum Disorder: A Randomized Controlled Trial

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Abstract

Pivotal Response Treatment (PRT) is promising for children with Autism Spectrum Disorder (ASD), but more methodologically robust designed studies are needed. In this randomized controlled trial, forty-four children with ASD, aged 9–15 years, were randomly allocated to PRT ($n = 22$) or treatment-as-usual (TAU; $n = 22$). Measurements were obtained after 12- and 20-weeks treatment, and 2-month follow-up. PRT resulted in significant greater improvements on parent-rated social-communicative skills after 12 weeks treatment ($p = .004$, partial $\eta^2 = 0.22$), compared to TAU. Furthermore, larger gains in PRT compared to TAU were observed on blindly rated global functioning, and parent-rated adaptive socialization skills and attention problems. Implications for clinical practice and suggestions for future research are discussed.

Keywords Autism spectrum disorder (ASD) · Pivotal response treatment (PRT) · Randomized controlled trial · School-age · Adolescents

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder characterized by deficits in social communication and interaction, the presence of repetitive and restricted patterns of behavior, interests or activities, and sensory abnormalities (American Psychiatric Association 2013). At present, most children with ASD are referred and diagnosed during the late preschool years or even later (van 't Hof et al. 2020). Having access to effective intervention programs is of high importance, since this may improve the outcome of ASD significantly (Dawson and Bernier 2013).

There is a wide range of behavioral and educational interventions available for children with ASD. In the current

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clinical practice, promising interventions are based on the principles of Applied Behavior Analyses (ABA) and developmental strategies – such as Naturalistic Developmental Behavioral Interventions (NDBI's; Schreibman et al. 2015). The emphasis of these type of interventions is on the integration of knowledge and skills across developmental domains and on generalization of learned skills at every phase of the intervention. Also, in contrast to other approaches such as traditional ABA, implementation in the child's natural environment is a core component of NDBIs, which enforces generalization to daily routines (Schreibman et al. 2015). A prominent NDBI with emerging evidence is Pivotal Response Treatment (PRT). In this treatment the focus is on targeting "pivotal" areas (i.e. motivation for social contact, self-initiations, self-management, and responding to multiple cues) that may contribute to gains in the child's other domains of functioning and responding, such as joint attention and eye contact (Koegel and Koegel 2006). PRT strategies are child-focused and have a natural rewarding approach to strengthen the child's motivation for social contact. Implementation procedures include: following the child's interests, gaining the child's attention, using clear instructions (prompts), providing immediate and contingent reinforcement in response to a child's initiation or good attempt, and interspersing maintenance and acquisition tasks. PRT can

be implemented by a broad range of providers such as clinicians, parents, and teachers and the treatment is not limited to the individual's age or level of abilities (Koegel and Koegel 2006). Therefore, PRT facilitates easily adaptation to individual target behavior, ongoing intervention in everyday situations and generalization of the acquired skills.

Although PRT is not age-restricted, PRT is mainly been studied in preschool-aged children with ASD or children with ASD and intellectual disability (Ona et al. 2019; Verschuur et al. 2014). The results of most of these studies provide support for the use of PRT to increase self-initiations and collateral improvements in communication and language, play skills, affect and adaptive functioning (e.g. Baker-Ericzén et al. 2007; Koegel et al. 1999; Stahmer 1995). Furthermore, several studies showed that PRT facilitates parent–child interactional patterns (Nefdt et al. 2010) and decreases parental stress (Minjarez et al. 2013). The few studies that investigated the efficacy of PRT in school-aged children and adolescents suggest improvement in social initiations, turn-taking, question-asking (Doggett et al. 2013; Huskens et al. 2012; Verschuur et al. 2017; Harper et al. 2008) and interactions with peers (Brock et al. 2018; Pierce and Schreibman 1995). However, these studies had a large variety in treatment intensity and PRT providers (peer- vs. parent- vs. clinician), small sample sizes ($n = 2$–14), and in most studies a control group was lacking. As far as known, only two randomized controlled trials (RCTs) have been conducted on PRT for school-aged children. Of these, one trial compared clinician (speech/language specialist) delivered PRT with highly structured, applied behavior analysis (ABA) (Mohammadzaheri et al. 2014, 2015). In the other trial, clinician (speech/language specialist) delivered PRT in combination with risperidone was compared with treatment with only risperidone (Rezaei et al., 2018a, 2018b). In both trials PRT was more effective in improving social communication and also resulted in gains in other areas, such as decreased behavioral problems. However, parents and teachers were not involved in the treatment protocol which might have a negative impact on the maintenance of skills and generalization to the naturalistic environment.

In summary, evidence on the efficacy of PRT for school-aged children and adolescents with ASD is limited. To address this gap in the literature, the aim of the current study was to examine the efficacy of clinician-delivered PRT in school-aged children and adolescents with ASD, integrating parent training and involvement of teachers. This study incorporated a RCT design, including blinded and non-blinded outcomes, a flexible endpoint of treatment duration and a 2-month follow-up assessment. More specifically, this study focused on examining the efficacy of PRT compared to treatment-as-usual (TAU) in: (1) improving general social-communicative skills, (2) improving global- and adaptive functioning, lowering severity of ASD symptoms,

behavioral and emotional problems and parenting stress, and (3) exploring child- and intervention-related factors that may modify treatment outcome. It was hypothesized that both PRT and TAU would result in positive treatment outcomes, with larger gains in the PRT group.

Methods

Study Design

A RCT design was used to investigate the efficacy of PRT compared to TAU (Dutch trial register number NL5476/NTR5893 (2016-06-10), full protocol is available on request), with a treatment allocation ratio of 1:1. The study was conducted at Karakter, a multi-site expert center for child and adolescent psychiatry in The Netherlands. In total, six sites (Nijmegen, Arnhem, Tiel, Uden, Zwolle, Hengelo) were involved in the study, all using the same clinical protocols. A digitalized program (Castor 2019) was used for random sequence generation. Treatment allocation could not be foreseen by any of the investigators. Sample size calculation was based on a small pilot study on the effectiveness of PRT for children aged 3–8 years old with ASD (Duifhuis et al. 2017). In this pilot study PRT resulted in larger improvements on total scores of the Social Responsiveness Scale (SRS; Constantino and Gruber 2005) compared to treatment-as-usual (pre-treatment vs. post-treatment mean difference change score; PRT = 10.5 and TAU = 2.0). Because of a more rigorous research design in the current study, a larger mean difference change score within the PRT group was expected compared to the change score in the TAU group (12.0). Therefore, it was estimated that for both groups 19 participants would be sufficient in having 80% power (with $\alpha = 0.05$) to detect a treatment effect with an effect size of $d = 0.95$ (Browner et al. 2013; Fleiss et al. 1980). To account for attrition, extra participants were included in each group. The study was approved by the Local Ethics Committee (CMO Arnhem-Nijmegen, NL54706.091.15).

Participants

Participants were recruited between June 2016 and March 2018. The inclusion criteria were: (1) a clinical diagnosis of ASD based on the DSM-IV-TR (American Psychiatric Association 2000) or DSM-5 (American Psychiatric Association 2013) and multidisciplinary assessment; (2) aged 9–15 years at start of the study; (3) a total intelligence quotient (TIQ) of 80 or higher; and (4) at least one Dutch speaking parent. The exclusion criteria included specific comorbid problems of participants that required a major intervention, family and parental factors that interfered with the PRT such as severe parental psychopathology, distorted family communication

or no parental acceptance of the ASD diagnosis, and/or having received PRT in the past. For participants in the PRT group, fixed medication dosage before start of the intervention was required. However, when medication dosages had to be changed during the intervention, participants were not excluded from the study due to the intention-to-treat (ITT) approach. See Table 1 for an overview of medication use in both groups.

Measures

Demographic Information and Baseline Measures

Demographic data of participants (i.e. age, sex, psychiatric comorbidity, and medication use) were gathered from case files of Karakter. The Dutch version of the Wechsler Intelligence Scale for Children -third edition (WISC-III-NL; Kort et al. 2005) was used for the assessment of IQ of the child (the WISC-IV (Wechsler 2003) was not available for the Dutch population). After the first treatment appointment, parents and participants aged $\geq$ 12 years old were asked

to rate their expectancies about treatment outcome on a 1-item *treatment expectancy scale* ranging from 0 to 9, with a higher score representing higher expectancies in treatment outcome. The purpose of this scale was to examine if parents or participants had a personal preference for one of the treatment groups which may bias the parent-reported measures.

Primary Outcome Measure

Social Responsiveness Scale (SRS) General social-communicative skills (i.e. skills that the child shows in his/her natural environment) were measured using the Social Responsiveness Scale (SRS) total scores (Constantino and Gruber 2005). The 65-item digitalized questionnaire, rated on a 4-point scale, was administered by both the participant's parent and teacher at each time point. Total raw scores were used, with higher total scores indicating more impairment in general social-communicative skills.

Table 1 Participant baseline comparisons

	PRT			TAU				
	n	M	(SD)/%	*n*	M		(SD)/%	t/X^2 (df)	*p*
Age at baseline	22	11.87	(1.62)	22	11.70	(2.11)		− 0.29	.771
Sex								0.11	.741
Male	16	72.7	%	15	68.2	%			
Female	6	27.3	%	7	31.8	%			
TIQ	22	102.91	(14.93)	22	100.95	(12.24)		−0.48	.637
Educational level								0.09	.763
Primary	11	50.0	%	12	54.5	%			
Secondary	11	50.0	%	10	45.5	%			
Psychiatric comorbidity								5.69	.128
AD(H)D	5	22.7	%	7	31.8	%			
AD(H)D + other	1	4.5	%	1	4.5	%			
Other	5	22.7	%	0	0.0	%			
Medication use								0.53 (3)	.912
Stimulants	6	27.3	%	4	18.2	%			
Stimulants + antipsychotics	1	4.5	%	1	4.5	%			
Antipsychotics	1	4.5	%	1	4.5	%			
Treatment expectancy scale									
Parent	21	6.62	(1.36)	9	6.67	(1.36)		0.09	.931
Child[a]	5	5.20	(3.11)	3	6.33	(1.53)		0.58	.585
ADOS-2 CSS	21	5.00	(1.87)	22	5.95	(1.33)		− 1.93	.062
CGI- severity	22	4.73	(0.94)	22	4.45	(0.96)		− 0.95	.346

ADOS-2 CSS; Autism diagnostic observation scale-second edition calibrated severity score, *AD(H)D*; Attention deficit (hyperactivity) disorder, *Antipsychotics*; Risperidone/Aripiprazole, *CGI-severity*; Clinical Global Impression-severity scale, *Stimulants*; Methylfphenidate/Dexamphetamine, *TIQ*; Total Intelligence Quotient

[a]Child $\geq$ 12 years old

Secondary Outcomes Measures

Clinical Global Impression-Improvement (CGI-I) Blindly Rated Change in clinical global functioning was examined at week 10 (to determine if extension of 8 weeks was necessary after 12 weeks intervention), week 20 and week 28 by the CGI-I scale (Guy 1976). The CGI-I was rated on a 7-point scale (*very much improved – very much worse*) by an experienced child- and adolescent psychiatrist blinded to group assignment. In total, two psychiatrists were involved for the ratings, who were unfamiliar with the participant and based their rating on information about clinical status of overall functioning, symptoms, and well-being in major areas of the participants life (i.e. home, school, relationships). The psychiatrists obtained this information from clinicians who were aware of the current clinical status of the child but not directly involved in the therapy (i.e. coordinating therapist). The clinicians were instructed not to disclose information on treatment status. Clinical responders were defined as participants that were rated as *very much improved* (score 1) or *much improved* (score 2).

Autism Diagnostic Observation Schedule-Second Edition (ADOS-2) Blindly Rated Severity of ASD-related symptoms were assessed at baseline and endpoint (week 12 or week 20) using the Dutch version of the ADOS-2 (De Bildt et al. 2013), Modules 3 and 4. The ADOS-2 was performed by a certified clinician who was unfamiliar with the participant, and blinded to group assignment and earlier outcomes on the ADOS-2. Calibrated severity scores (CSS; Gotham et al. 2009) were calculated, with higher scores indicating more severe ASD symptoms. For comparability across modules, a revised Module 4 algorithm with provided calibrated severity scores was used (Hus et al. 2014).

Vineland Adaptive Behavior Scales- Second Edition (Vineland-II) Adaptive functioning was assessed at baseline and endpoint (week 12 or week 20) using the Vineland-II, Survey Interview Form (Sparrow et al. 2005). The Vineland-II provides parent reported information using a semi-structured interview about child's everyday adaptive functioning on different domains: Communication, Daily living skills, and Socialization. Parents were interviewed by independent clinicians who were trained and certified in the use of the Vineland-II, and who regularly attended consensus meetings. The clinician who assessed the interview was blinded to group assignment and earlier outcomes on the Vineland-II and was unfamiliar with the participants. The overall adaptive behavior composite (ABC) standardized score as well as the domain scores were used, with higher scores indicating better adaptive skills.

Brief Problem Monitor-Parents (BPM-P) Internalizing-, externalizing-, attention-, and total behavioral and emotional problems were assessed at baseline, week 12 and week 20 using the digitalized BPM-P (Achenbach et al. 2011). The BPM-P is an abbreviated version of the Child Behavior Checklist and consists of 19 items, rated on a 3-point scale (*not true-very true)* by parents. Total- and domain T-scores were computed and used for analyses, with higher scores indicating more behavioral and emotional problems.

Parenting Stress Questionnaire (OBVL) Parenting stress was assessed at all time points, using the digitalized 34-items Dutch Parenting Stress Questionnaire "Opvoedingsbelastingvragenlijst" (OBVL; Vermulst et al. 2012). The OBVL contains five scales: Problems in parenting, Problems in parent–child relation, Depressive mood, Role-restriction, and Health complaints. Parents rated whether the items were applicable to them on a 4-point scale. Total T-scores were computed and used for analyses, with higher scores indicating more parenting stress.

Procedures

Child- and adolescent psychiatrists and psychologists of Karakter referred potential participants for enrollment in the study. Verbal and written information on the aim, outline and time investment of the study was provided to participants and their parents. Assessment of IQ was done if assessment was not available in case files within 2 years before enrollment. After evaluating study eligibility, written informed consent was obtained from parents (and participants when ≥ 12 years old) and the participants were randomly assigned to either PRT or TAU. Before start of the intervention phase and baseline measures, all participants and parents received psycho-education on ASD (if applicable by indication and not received earlier). The child's teacher was informed about the study by e-mail and was asked to complete questionnaires online. To explore the optimal intervention intensity of PRT, the intervention phase of the study had a flexible duration and was initially 12 weeks. When participants were rated as not "much improved" or "very much improved" on the Clinical Global Impression- Improvement scale (CGI-I; see measures), the intervention phase was extended with 8 weeks. All participants were assessed at four similar time points: week 0 (baseline) week 12, week 20, and week 28 (2-month follow-up).

Pivotal Response Treatment (PRT)

Participants in the PRT condition received treatment according to a written protocol based on the PRT principles (Koegel and Koegel 2012), provided by a certified PRT therapist. In total, six PRT therapists were involved in the study. PRT principles included (a) child's choice, (b) interspersing maintenance and acquisition tasks, (c) task variation, (d) natural and direct rewards, and (e) rewarding attempts. The treatment focused on creating different social communication learning opportunities for the child (depending on individual target goals) and on teaching parents and teachers to implement PRT principles in the natural environment of the child. Learning opportunities were created using a three-term contingency: (1) antecedent stimulus (i.e. following child's choice in selecting activities/materials/subject of conversation, catching the child's attention, providing clear opportunity with appropriate prompts, and interspersing maintenance and acquisition tasks), (2) goal behavior (i.e. the child's self-initiation), (3) reinforcing the child's self-initiation or appropriate attempt naturally and contingently. An intervention protocol of 12 weekly sessions was used including seven parent–child sessions, three parent-only sessions, and two sessions in which the child's teacher was involved. If intervention was extended with 8 weeks, four parent–child sessions, two parent-only sessions, and one session with the teacher were added. Prior to the sessions the therapist informed parents and children about the treatment and discussed the child's individual target goals in social communication, according to the child's needs and interests. Because of the age range in this study, individual target goals could relate to functional communicative intentions (e.g. asking for an object/activity, asking for help, protesting) and/or social communicative intentions (e.g. starting and maintaining social conversation; asking for social information, asking for opinion, commenting). See Supplement 1 for examples of PRT learning opportunities on these subtypes of individual target goals. Each PRT session had a duration of 45 min, except for one teacher session which included a 90 min school visit (if applicable). In the parent–child sessions the therapist demonstrated the PRT techniques and coached parents in applying the techniques during parent–child interaction (e.g. playing a game, drawing, conversations). When more appropriate for the child's individual goal (e.g. starting and maintaining social conversation goal for children aged ≥ 12 years old), techniques were implemented during a triadic clinician-parent-adolescent interaction rather than during only parent–child interaction. The parent–child sessions were recorded on video. In the parent-only sessions video segments were discussed and the child's goals were evaluated. Also, the implementation of PRT in the naturalistic environment was discussed. Children could attend these sessions (partly) if this would contribute to their skill development. During the teacher sessions the therapist instructed the teacher how PRT techniques could be implemented to facilitate child's social communication at school.

Treatment-As-Usual (TAU)

Participants in the TAU condition received outpatient treatment that was indicated by a clinician based on 'shared decision making' with participants and their parents. The TAU condition consisted of guidance of parents, (intensive) family therapy, social skill training (group or individually), cognitive behavior therapy, (change in) pharmacotherapy, or a combination of these. Intensity and frequency of these treatments differed (ranging from 1.5 h per week to 1 h per month). If there was no clinical indication for one of these treatments, progress was monitored during a waiting list period. Since TAU was based on the participant's specific needs during the intervention phase, duration of TAU was—in comparison to PRT- not based on CGI-I ratings of week 10. After an intervention period of 12 weeks all participants in the TAU group could receive PRT.

Statistical Analyses

Statistical analyses were performed with SPSS Statistics (IBM-Corp. 2017), with a significance level set at $p = 0.05$. Demographic characteristics and baseline measures of both groups were assessed with Independent Samples T-tests and Chi-square tests. Little's MCAR test (Little 1988) confirmed that missing data were 'missing completely at random' [$\chi 2$ $(671) = 598,157$, $p = 0.980$]. All outcome measures had a missing rate of less than 20%. Missing values were imputed, using the expectation–maximization technique (Schafer and Graham 2002). Results based on complete cases are reported, since imputation did not alter conclusions.

To examine differences between groups (PRT vs. TAU) over time (weeks 0, 12, 20 and 28) on the continuous outcomes, a repeated measures analysis of variance analysis (ANOVA) was conducted. Significant time x group interaction effects were explored by a priori contrasts between weeks. To examine differences between groups (PRT vs. TAU) over time (weeks 0, 12, 20 and 28) on the categorical outcomes, Chi-square tests were conducted. Assumptions were checked before all analyses. If the assumption of normality of residuals was violated, outliers were converted to two standard deviations from the mean. All criteria for parametric testing were met, except for the following secondary outcomes: ADOS total scores and calibrated severity scores, Vineland Socialization and Daily Living Skills subscale scores, and all BPM-P scores. For these outcomes the assumption of normality of residuals was violated, even after correction for outliers. To assess effects on these outcomes, non-parametric Friedman tests

were computed for within-group analyses over time and Mann–Whitney U tests were computed for between-group analyses (using change scores between baseline-endpoint). Bonferroni-holm corrections (Holm 1979) on secondary outcomes were applied to account for multiple testing.

The association between child-related (i.e. sex, age, IQ, and ASD symptom severity) characteristics and the primary outcome measure were also explored by examining Spearman correlations between these variables. Furthermore, additional analyses were performed to examine intervention-related characteristics (intensity and
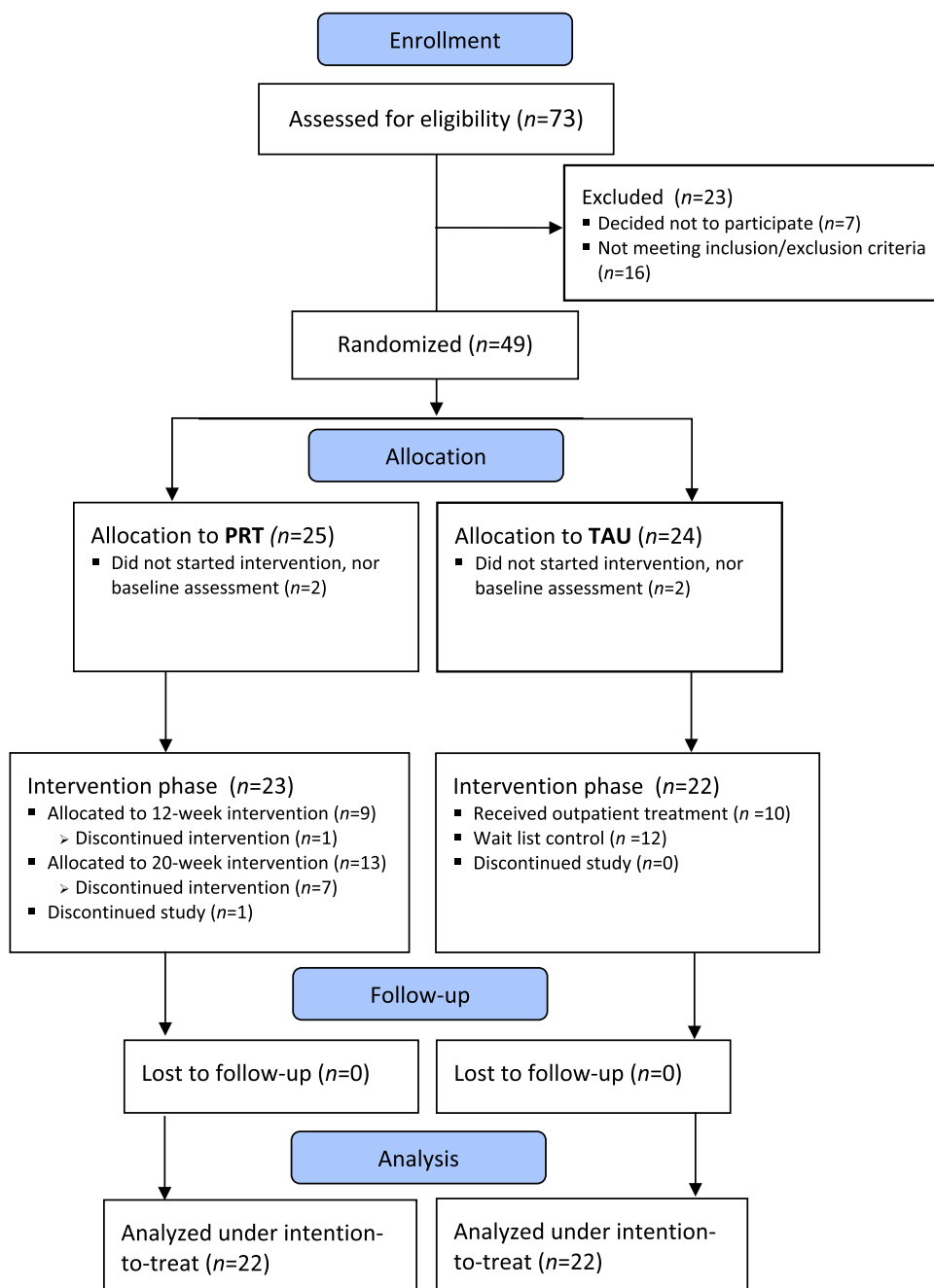
duration). An intention-to-treat (ITT) approach was used for all analyses.

Results

Study Population

Figure 1 presents the CONSORT participant flow diagram. In total, 49 participants were randomized to either PRT (n=25) or TAU (n=24). In each group, two participants did

**Fig. 1** CONSORT participant flowchart

not start with the allocated intervention and/or not received baseline assessment, resulting in 45 participants that initiated the allocated intervention. One participant discontinued the study during the intervention phase, resulting in a total sample of 44 participants. In the PRT group, nine participants were allocated to the 12-week intervention and thirteen participants were allocated to the extended 20-week intervention, based on CGI-I ratings. However, one participant discontinued the intervention before the indicated 12-week intervention, because of achieved goals in social communication skills. Furthermore, seven participants discontinued the intervention before the allocated 20-week intervention, due to (1) lack of motivation of the participant to continue intervention ($n = 4$), or (2) a need to switch to another intervention for comorbid problems ($n = 3$). However, the participants who discontinued the PRT group before the allocated 12-week or 20-week intervention completed all the assessments. In total, 18 of the 22 participants (82%) followed ≥ 12 weeks of PRT intervention. In the TAU group, 10 participants received outpatient TAU (TAU-treatment; 30% social skill training, 20% cognitive behavior therapy, 10% change in pharmacotherapy, 10% guidance of parents/(intensive) family therapy, and 30% a combination of these), and 12 participants received no additional outpatient treatment after psycho-education but were monitored during a waiting list period (TAU-wait list). Two participants in the TAU group started with PRT after a 12-week waiting list period (one at week 13 and one at week 17) and three participants started with PRT after 20 weeks. Because of variety in the total TAU group there was a significant difference in mean hours of treatment between groups (PRT; M = 11.18 (SD = 4.08), TAU; M = 4.66 (SD = 6.89), $p < 0.01$). However, when comparing PRT with the TAU-treatment group, there was no significant difference in mean hours of treatment (PRT; M = 11.18 (SD = 4.08), TAU-treatment; M = 9.46 (SD = 7.83), $p = 0.42$). All participants continued the assessments and were analyzed based on the intention-to-treat (ITT) model, with a total sample of 44 children (PRT: $n = 22$, TAU: $n = 22$). There were no significant group differences in any of the baseline characteristics (see Table 1) and also not in any of the baseline outcome measures. The results on the treatment expectancy scale indicated that expectancies on both treatment groups were identical and there was no preference-based bias.

Primary Outcome Measure

SRS. Repeated measures ANOVA on the SRS rated by parents revealed a significant main effect of time ($F (3,102) = 8.15$, $p < 0.001$, partial $\eta^2 = 0.21$), indicating a difference in general social-communicative skills across weeks in both groups (see Fig. 2). There was also a significant time x group interaction effect (see Table 2), with a priori contrasts demonstrating larger gains from baseline to week 12 for participants in the PRT group compared to TAU ($F (1,34) = 9.62$, $p = 0.004$, partial $\eta^2 = 0.22$). Although the increasing SRS scores from week 20 to follow-up in the PRT group suggest no further improvement in social-communicative skills, the difference between these time points was not statistically significant ($F (1,17) = 1.528$, $p = 0.233$, partial $\eta^2 = 0.08$). For the SRS rated by teachers, there was a significant main effect of time ($F (2.118,87) = 7.93$, $p < 0.001$, partial $\eta^2 = 0.22$), but no significant time x group interaction effect.

Fig. 2 Parent-rated SRS scores between PRT and TAU at all time points, with error bars representing standard errors. Group differences were observed at week 12 ($F (1, 34) = 9.62$, $p = 0.004$, partial $\eta^2 = 0.22$)
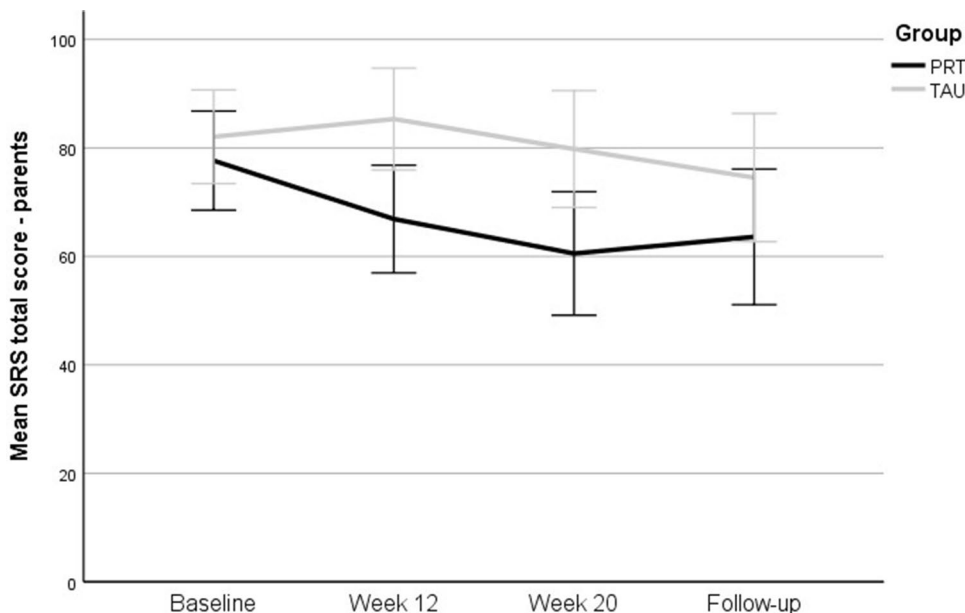
Table 2 Interaction effects on the SRS, CGI-I, BPM-P and OBVL across time points between the PRT and TAU group

Measure	PRT (n=22)				TAU (n=22)				Interaction-effect[a]		
	Baseline M (SD)	Week 12 M (SD)	Week 20 M (SD)	Follow-up M (SD)	Baseline M (SD)	Week 12 M (SD)	Week 20 M (SD)	Follow-up M (SD)	F(df)/U	p	η2
SRS total score											
Parent (n=17–19)*	77.65 (11.97)	66.88 (20.01)	60.53 (20.65)	63.59 (22.51)	82.05 (22.83)	85.32 (20.26)	79.79 (25.08)	74.53 (27.65)	3.92 (3)	**.012**	0.10
Teacher(n=12–19)*	87.58 (25.59)	70.25 (25.93)	70.92 (33.16)	69.75 (28.90)	76.47 (34.79)	65.74 (29.68)	60.95 (23.67)	58.47 (27.68)	0.30 (3)	.752	0.01
CGI-I (n=22–22)*											
Score	–	2.40 (0.88)	1.95 (1.10)	1.75 (1.02)	–	3.33 (1.16)	2.90 (1.18)	3.10 (1.48)	0.97	.384	0.02
Clinical responder %	–	40.90	63.60	80.00	–	31.80	42.90	45.50	–	–	–
BPM–P (n=18–22)*											
Total t score	60.44 (5.80)	57.56 (6.47)	55.00 (5.86)	–	59.69 (6.46)	60.50 (6.16)	59.00 (5.96)	–	125.00	.043	–
Internalizing	59.00 (6.95)	56.50 (6.10)	55.15 (6.67)	–	62.35 (6.17)	61.40 (6.03)	60.10 (6.50)	–	180.50	.602	–
Externalizing	57.59 (6.02)	55.59 (5.47)	55.58 (5.47)	–	56.77 (6.57)	57.41 (4.90)	57.41 (4.91)	–	173.00	.478	–
Attention	60.72 (6.78)	58.83 (7.23)	56.28 (6.06)	–	58.24 (7.17)	60.06 (8.41)	58.28 (7.33)	–	107.50	**.011**	–
OBVL t-score (n=17–19)*	58.47 (9.78)	55.41 (10.91)	55.94 (11.34)	54.41 (12.08)	58.84 (9.16)	62.53 (8.63)	60.37 (10.78)	58.05 (12.91)	2.36 (3)	.080	.06

Bold font indicates statistical significance at $p < 0.05$

* n=number of participants (PRT–TAU) with complete assessments of all time points

[a] Interaction-effect of RM ANOVA (F) or Mann–Whitney tests (U)

Secondary Outcome Measures

CGI-I blindly rated. The CGI-I continuous score revealed no significant group differences on the child's improvement in clinical global functioning (see Table 2). The proportion of clinical responders on the CGI-I was higher in PRT compared to TAU, but chi-square statistics did not reach statistical significance between both groups at week 12 or week 20 (p's > 0.05). At week 28 (2-month follow-up) there was a significant treatment effect, with a higher proportion of clinical responders in the PRT group compared to the TAU group ($X^2 = 5.30$, $p = 0.021$). This result did not remain significant after correction for multiple comparisons.

ADOS-2 blindly rated. In 93% of all ADOS-2 assessments, a module 3 was administered. In the other 7% of the ADOS-2 assessments, module 4 was administered. Nonparametric Friedman tests indicated a significant decrease in observed ASD symptoms from baseline to endpoint in the total group on CSS scores (χ^2 (2) = 4.800, $p = 0.028$), see Table 3. Results of Mann-Whiney U tests showed that there were no significant group differences in baseline-endpoint change scores (CSS score; U = 196.500, $p = 0.925$).

Vineland-II. The overall Adaptive Behavior Composite score, the Communication subscale score and the Daily living skills subscale score did not change significantly over time or between groups (p's > 0.05), see Table 3. However, Mann–Whitney U tests showed significant group differences on the change in the Socialization subscale score (U = 99.500, $p = 0.002$). Participants in the PRT group showed significant improvement in adaptive socialization skills at endpoint (χ^2 (2) = 7.200, $p = 0.007$), but participants in the TAU group did not show significant changes in socialization skills (χ^2 (2) = 1.800, $p = 0.180$).

BPM-P. The non-parametric Friedman test demonstrated a significant decrease in the BPM-P total T-scores at week 20 in the total group (χ2 (2) = 14.936, $p = 0.001$). Furthermore, the Mann–Whitney U test resulted in significant group differences on the change (baseline-week 20) in the BPM-P total T-score (U = 125.000, $p = 0.042$), indicating a higher decrease in behavioral and emotional problems in the PRT group compared to TAU. Post-hoc analyses on BPM-P domains separately, revealed a significant difference between groups in the BPM-P Attention subscale, with a significant decrease in attention problems in the PRT group (χ^2 (2) = 11.556, $p = 0.003$), but not in the TAU group (χ^2 (2) = 3.679, $p = 0.159$). There were no significant treatment effects on the Internalizing and Externalizing subscale.

OBVL. No significant main effects of time or significant time x group interaction effects were found for total T scores, indicating no treatment effects on parenting stress.

Associations between Child Factors and Intervention Outcome

Exploratory analyses were conducted to examine whether child-related factors are associated with intervention outcomes on social-communicative skills (i.e. SRS). There were no significant correlations between age, sex or TIQ and treatment outcomes on the parent- and teacher- rated SRS (all p's > 0.05). However, there was a significant correlation between the baseline ADOS calibrated severity score and the change (baseline-week 20) on the parent-rated SRS total score in the total group (r_s (38) = 0.43, $p = 0.008$). Post hoc analyses indicated that this effect was specifically found for the PRT group (r_s (18) = 0.32, $p = 0.045$) and not for the TAU group (r_s (20) = 0.21, $p = 0.406$). More specifically,

Table 3 Interaction effects on the ADOS-2 and Vineland-II between baseline and endpoint for PRT and TAU

Measure	PRT (n = 22)				TAU (n = 22)				Interaction-effect[a]		
	Baseline		Endpoint		Baseline		Endpoint				
	M (SD)		M (SD)		M (SD)		M (SD)		F(df)/U	p	$\eta2$
ADOS-2 (*n* = 20–20)*											
CSS	4.95	(1.93)	4.40	(2.11)	6.15	(1.18)	5.40	(1.31)	196.50	.925	
Vineland-II (*n* = 20–22)*											
ABC	80.14	(8.00)	81.76	(8.77)	80.38	(6.28)	80.00	(5.76)	1.95	.171	0.05
Communication	80.82	(12.18)	79.95	(10.36)	79.70	(7.90)	77.20	(8.75)	0.35	.559	0.00
Daily living skills	85.55	(8.81)	82.82	(8.44)	84.43	(9.73)	86.30	(9.20)	154.50	.063	
Socialization	81.37	(7.85)	88.43	(11.26)	83.51	(6.50)	83.19	(6.47)	99.50	**.002**	

Bold font indicates statistical significance at $p < 0.01$

CSS; Calibrated Severity Score, *ABC*; Adaptive Behavior Composite score

* n = number of participants (PRT-TAU) with complete assessments of all timepoints. Endpoint represents either week 12 or week 20

[a] Interaction-effect of RM ANOVA (F) or Mann–Whitney tests (U)

for the PRT group lower severity of ASD symptoms was associated with greater improvement on parent-rated social-communicative skills. There was no significant correlation between the baseline ADOS calibrated severity score and the teacher-rated SRS total score.

To check whether significant differences between PRT and TAU on improvement in social-communicative skills were not purely driven by treatment intensity, additional post-hoc analyses on the SRS were performed in which the PRT group was compared with the TAU group that received outpatient treatment (TAU-treatment) and with the TAU group that received no outpatient treatment (TAU-wait list) during the intervention phase of the study. Results indicated significantly larger improvement on the parent-rated SRS from baseline to week 12 in the PRT group compared to both the TAU- treatment group ($p = 0.013$, partial $\eta 2 = 0.238$) and the TAU-waitlist group ($p = 0.025$, partial $\eta 2 = 0.179$). The treatment duration comparison analyses showed that there were no significant group differences in treatment outcomes for participants receiving either 12 weeks or 20 weeks of PRT. Finally, analyses with exclusion of participants that initiated PRT after 12 weeks in the TAU group ($n = 2$) did not alter conclusions.

Discussion

This study represents the largest RCT to-date on the efficacy of PRT in school-aged children and adolescents with ASD, including parent-, teacher- and blinded clinician ratings, a flexible endpoint of PRT treatment duration and a two month follow-up assessment. In this study PRT consisted of clinician-delivered treatment, with intensive parent training and active involvement of teachers. As hypothesized, the results indicated positive treatment effects for both groups, with larger gains for children and adolescents receiving PRT. Children receiving PRT demonstrated significantly larger improvement in parent-rated general social-communicative skills after 12 weeks of intervention, compared to children receiving TAU. PRT also resulted in a higher percentage of clinical responders on global functioning and a higher decrease in behavioral and emotional problems. Furthermore, in comparison to TAU, collateral improvements in adaptive socialization skills were observed in the PRT group. For severity of ASD symptoms observed on the ADOS-2 there was a similar decrease in PRT and TAU and there were no treatment effects on parenting stress. In general, these findings provide support for PRT as an established intervention for school-aged children and adolescents with ASD.

The observed improvement in general social-communicative skills in this study is consistent with previous findings on the efficacy of PRT in social communication outcomes (Hardan et al. 2015; Mohammadzaheri et al. 2015, 2014;

Schreibman and Stahmer 2014). Current results indicated that the benefits for PRT compared to TAU on general social-communicative skills were based on parent ratings and not on teacher ratings. A possible explanation for these mixed results is that child's gains in social communication skills did not generalize to the school setting, since children with ASD have difficulties in generalizing learned skills to a new environment (de Marchena et al. 2015). Children with ASD might need more support and training at school to show significant gains in social communication in this environment. In the current study, the main focus was on parent and child/adolescent training during the treatment. Parents were involved in the determination and evaluation of the child's target skills in social communication and attended all sessions, which may have facilitated generalization to daily in-home situations. Teachers were far less involved in the treatment. Furthermore, teachers had less individual interaction with their students ─ half of the participants followed education at secondary schools ─ causing considerably lower one-to-one contact of the child/adolescent with the teacher. Therefore, an alternative explanation for the incongruence in parent and teacher ratings is that the teachers' possibility to observe and identify (change in) skills might have been limited.

A higher percentage of blindly rated clinical responders in clinical global functioning (CGI-I) was observed for the PRT group compared to the TAU group, although this difference only reached significance at two month follow-up and significance did not remain after multiple comparison correction. These results are in contrast with previous RCTs indicating additional gains resulting from PRT in clinical global functioning directly after treatment (Gengoux et al. 2019; Hardan et al. 2015). The inconsistency in findings may be due to age differences among study samples and how ratings were established. Current findings may point to the possibility of ongoing improvement in clinical global functioning after PRT intervention. A larger treatment difference at follow-up compared to post-treatment, often referred as sleeper effect, is common across psychotherapy trials and indicates that time is needed for an intervention to results in (more) benefits (Flückiger and Del Re 2017). Future research on PRT with follow-up assessments is warranted to explore the possibility of a sleeper effect in the effectiveness of PRT.

The results of the blinded clinician-reported ADOS-2 revealed no significant group differences in treatment outcome, which is in contrast with previous research reporting lower severity of ASD symptoms after PRT compared to TAU or a wait list comparison group (Vernon et al. 2019; Duifhuis et al. 2017). This discrepancy in findings may be due a relatively short time between baseline and endpoint assessment in the current study (12 weeks for most participants, compared to 24 or 26 weeks in previous studies), considering that the ADOS-2 is limited to detect changes over

shorter periods of time (Pijl et al. 2018). To date, the Brief Observation of Social Communication Change (BOSCC) is upcoming as an outcome measure in clinical trials, since it might be a more sensitive measure for capturing change of ASD symptoms (Gengoux et al. 2019; Pijl et al. 2018). However, subsequent evaluation of this new instrument and application for school-aged children and adolescents will be needed to explore the advantages of the BOSCC as an outcome measure of ASD symptoms in intervention studies.

Interestingly, participants with a lower severity of ASD symptoms at baseline were associated with greater improvement on parent-rated general social-communicative skills. To date, there is lack of evidence on effects of specific child-related factors on treatment outcome of PRT (Fossum et al. 2018), which limits the comparison with other studies. However, previous research on ASD interventions for preschool-aged children indicates that lower severity of ASD symptoms is related to higher treatment outcome in adaptive communication skills, language skills and play skills (Ben-Itzchak and Zachor 2007; Zachor and Ben-Itzchak 2010). The current study demonstrated that severity of ASD symptoms seems to contribute to social communication skills among school-aged children and young adolescents with ASD as well. Additional research with higher sample sizes and different age groups is warranted to further identify which individually- and family-related factors contribute to higher benefits of PRT.

To explore the optimal intervention dosage of PRT, the intervention phase of PRT had a flexible duration and could be extended after 12 weeks, based on accurate blinded clinician CGI-I ratings. The results indicated that there were no significant differences in improvement of general social-communicative skills between participants who followed the 12 week or 20 week PRT treatment. However, it was remarkable that some participants did not continue the intervention, even though CGI-I ratings provided indication for an extension of PRT. The most common reason was a lack of prolonged motivation of the participant to improve further social communication skills. This can be explained by the age group of this study. In older children and adolescents, in contrast to preschool-aged children, it is more challenging to capture and maintain motivation for interaction, since their awareness and understanding of their deficits in social-communicative behavior is limited (Huang et al. 2017) and their susceptibility to adhere to their parents' wishes is lower. Therefore, lessons learned from this study are that (1) a strong internal motivation of the adolescent to improve social-communicative skills is very important, and that (2) PRT for school-aged children and adolescents may require adjustments in ways of delivery, for instance by higher focus on implementation of PRT techniques in self-chosen leisure activities and interests (e.g. music- arts- and/or sports-related activities) and higher involvement of peers.

The participants in the PRT group demonstrated, compared to TAU, significant lower behavioral and emotional problems as reported by parents. This was particularly reflected by less attention problems. Furthermore, parents observed improvements in adaptive socialization skills after PRT treatment but not after TAU. These findings are in line with previous reports on collateral gains after PRT (Gengoux et al. 2019; Ventola 2016; Ventola et al. 2014) and suggest optimism that also for school-aged children and adolescents PRT contributes to (1) generalization and adaptation of learned skills across the everyday environment and (2) collateral improvements in comorbid symptoms such as attention problems.

There were no treatment effects in reducing parenting stress in both treatment groups. Mixed findings have been reported in previous studies, with similar results in the study of Duifhuis et al. (2017) and Stock et al. (2013), and different results compared to the study of Minjarez et al. (2013) and Verschuur et al. (2019) in which there was a significant decrease in parenting stress after PRT. A treatment-enhancing component in these last two studies might have been the implementation of a parent group within PRT, facilitating the ability of parents to share their experiences on the impact of having a child with ASD. Sharing experiences with parents in similar circumstances may result in social support and can have a positive impact on parenting stress (Minjarez et al. 2013). Furthermore, since parenting stress is considerably related to the overall impact of having a child with ASD (i.e. life-long concerns, comorbid problems, feelings of loss and grief), complementary parent-focused interventions might be important to optimize family outcomes (Keen et al. 2010).

While the results of this study are promising, several limitations should be noted. First, the flexible endpoint of treatment duration in PRT and variability in kind and intensity of TAU led to a highly representative patient-tailored treatment, but also to an increase in heterogeneity within both treatment groups. Specifically for the TAU group, there was a subgroup of participants that actually received outpatient intervention and participants that were monitored during a waiting list period. Post-hoc analyses were conducted to account for this heterogeneity in treatment intensity. Additionally, this study incorporated a combination of clinician-delivered PRT, parent training and involvement of teachers and therefore included multiple treatment providers. Because previous research on the efficacy of PRT for school-aged children and adolescents is lacking, the possibility to identify which treatment providers are essential for optimal outcome is limited. Nowadays, the use of typically developing peers as treatment provides – often named as peer-mediated PRT (PM-PRT) – is also considered as a promising treatment approach since it facilitates ongoing practice in the context of naturally occurring routines (Boudreau et al.

2015). Besides the use of peers as treatment providers, peers might also be additional valuable for reports on measuring changes in social communication of school-aged children and adolescents. Future research should explore the role of peers in the implementation of PRT. Another limitation was the relatively broad range in age in this study, resulting in a diverse set of individual target behaviors in social-communicative skills. Therefore, some adaptations to the protocolized parent–child sessions existed in which there was a clinician-parent-adolescent triad of practicing social conversations, rather than parent–child game play. This variability among sessions complicated assessment of parental fidelity of PRT implementation and could therefore not be truly assessed in this study. Furthermore, there was a high emphasis on parent implementation of PRT techniques during daily routines at home, rather than intensively during a video-recorded 10 minute parent–child interaction which would have facilitated fidelity scoring. Lastly, no long-term follow-up assessments were conducted in this study. Although this study serves as a first step by including a short-term follow-up, this follow-up period should be extended in future studies to explore generalization and maintenance of both targeted and collateral skills.

As most of the studies have focused on the efficacy of PRT for young children with ASD, the current study demonstrates that PRT may be a promising treatment for improving social-communicative skills and collateral improvements in older children and adolescents. Additional research is needed to further support evidence for use of PRT in this age group and to understand the individual- and treatment-related (duration, intensity, method of delivery) predictors contributing to optimal intervention outcomes for school-aged children and adolescents with ASD.

Compliance with Ethical Standards

Conflict of interest Jan K. Buitelaar has been in the past three years a consultant to/member of the advisory board of/and/or speaker for Takeda/Shire, Roche, Medice, Janssen Cilag, Angelini, and Servier. He is not an employee of any of these companies, and not a stock shareholder of any of these companies. He has no other financial or material support, including expert testimony, patents, and royalties. All other authors declare that they have no conflict of interest.

Ethical Approval All procedures performed in this study involving human participants were in accordance with ethical standards of the institutional and national research committee an with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Consent to Participate Informed consent was obtained from the parents (and participants when ≥ 12 years old) included in this study.

Consent to Publish All parents (and participants when ≥ 12 years old) included in this study signed informed consent regarding publishing their data.

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