cortex 85 (2016) 90–99

Available online at www.sciencedirect.com

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Behavioural neurology

Using language for social interaction: Communication mechanisms promote recovery from chronic non-fluent aphasia

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ARTICLE INFO

Article history:
Received 16 May 2016
Reviewed 15 July 2016
Revised 27 July 2016
Accepted 21 September 2016
Action editor Stefano Cappa
Published online 15 October 2016

Keywords:
Stroke
Aphasia
Intensive Language-Action Therapy (ILAT)
Constraint-Induced Aphasia Therapy (CIAT)
Formulaic language

ABSTRACT

Introduction: Clinical research highlights the importance of massed practice in the rehabilitation of chronic post-stroke aphasia. However, while necessary, massed practice may not be sufficient for ensuring progress in speech-language therapy. Motivated by recent advances in neuroscience, it has been claimed that using language as a tool for communication and social interaction leads to synergistic effects in left perisylvian eloquent areas. Here, we conducted a crossover randomized controlled trial to determine the influence of communicative language function on the outcome of intensive aphasia therapy.

Methods: Eighteen individuals with left-hemisphere lesions and chronic non-fluent aphasia each received two types of training in counterbalanced order: (i) Intensive Language-Action Therapy (ILAT, an extended form of Constraint-Induced Aphasia Therapy) embedding verbal utterances in the context of communication and social interaction, and (ii) Naming Therapy focusing on speech production *per se*. Both types of training were delivered with the same high intensity (3.5 h per session) and duration (six consecutive working days), with therapy materials and number of utterances matched between treatment groups.

Results: A standardized aphasia test battery revealed significantly improved language performance with ILAT, independent of when this method was administered. In contrast, Naming Therapy tended to benefit language performance only when given at the onset of the treatment, but not when applied after previous intensive training.

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http://dx.doi.org/10.1016/j.cortex.2016.09.021

Conclusions: The current results challenge the notion that massed practice alone promotes recovery from chronic post-stroke aphasia. Instead, our results demonstrate that using language for communication and social interaction increases the efficacy of intensive aphasia therapy.

1. Introduction

After decades of debate on the success of speech-language therapy (SLT) in neurological patients (Lincoln, McGuirk, Mulley, Jones, & Mitchell, 1984), clinical research has confirmed the relative efficacy of intensive regimes in the rehabilitation of chronic post-stroke aphasia (Brady, Kelly, Godwin, Enderby, & Campbell, 2016). In particular, a series of randomized controlled trials (RCTs) demonstrated the short- and long-term benefit from Intensive Language-Action Therapy (ILAT), an extended form of Constraint-Induced Aphasia Therapy, even if delivered years following the onset of the disease (Meinzer, Djundja, Barthel, Elbert, & Rockstroh, 2005; Pulvermüller et al., 2001; Szaflarski et al., 2015). Apart from its high intensity with up to 30 h of practice in less than two weeks, ILAT emphasizes the training of language skills in the context of communication and social interaction (Difrancesco, Pulvermüller, & Mohr, 2012).

Motivation for ILAT comes from linguistic theory, stating that the primary function of language emerges from its everyday use (Tomasello, 2005; Wittgenstein, 1953), and from neuroscience data. Crucially, recent studies revealed an increase of brain activity with communicative function, showing that requesting objects from a person elicits stronger neurophysiological and neuroimaging responses in cortical language and motor regions than picture naming performed with the same verbal utterances (Egorova, Pulvermüller, & Shtyrov, 2014; Egorova, Shtyrov, & Pulvermüller, 2013; Egorova, Shtyrov, & Pulvermüller, 2016). Further neuroscience evidence suggests that the neural bases of language and action are functionally interlinked (e.g., Glenberg, Sato, & Cattaneo, 2008; Pulvermüller, Hauk, Nikulin, & Ilmoniemi, 2005; Willems, Labruna, D'Esposito, Ivry, & Casasanto, 2011). Therefore, it has been argued that the co-activation of these neural systems potentially leads to synergistic effects (Pulvermüller & Fadiga, 2010), which might improve the outcome of SLT if verbal utterances are embedded in behaviorally relevant settings (Berthier & Pulvermüller, 2011). Still, the major variable currently seen as essential for the success of SLT in general, and ILAT in particular, is the intensity of the treatment, while the role of communication and social interaction remains not fully understood (Cherney, Patterson, Raymer, Frymark, & Schooling, 2008).

The present crossover RCT seeks to determine the impact of communication and social interaction on the efficacy of intensive SLT. Individuals with chronic non-fluent aphasia each received two types of intensive training in counterbalanced order: communicative-pragmatic action-embedded therapy focusing on verbal requests (ILAT), and utterance-centered confrontation naming (Naming Therapy). The design controlled for the influence of training intensity and duration, with therapy materials and number of utterances matched between treatment groups. According to traditional views in aphasia rehabilitation, the ability to name objects may be a precondition for successful communication, hence predicting that Naming Therapy should yield greater progress than ILAT (Shewan & Bandur, 1986). Conversely, linguistic theory and neuroscience data summarized above suggest that embedding verbal utterances in communication and social interaction may be key to facilitating language processing in left perisylvian eloquent areas, thus predicting better outcomes with ILAT than Naming Therapy.

2. Methods

2.1. Participants

Eighteen patients with a neurological diagnosis of chronic aphasia were eligible and agreed to participate in the current crossover RCT (for details, see Fig. 1). This sample size was consistent with a previous power analysis ($\alpha = .05$; $1-\beta = .95$; number of groups: 2; number of repeated measures: 3; estimated Cohen's $f = .4$, derived from Pulvermüller et al., 2001, and equivalent to an increase of two points per training period on our standardized aphasia test battery; cf. Faul, Erdfelder, Buchner, & Lang, 2009). All patients were native speakers of German who had not received intensive SLT in the year prior to inclusion in the study. Patients were aged 32–73 years (mean age: 51 years; standard deviation: 12 years) and right-

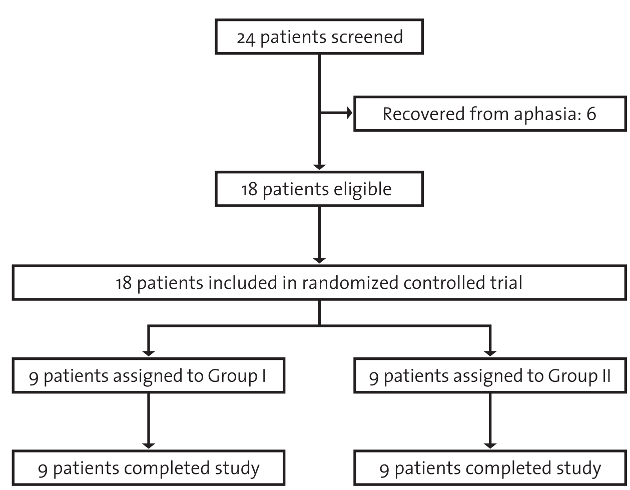

Fig. 1 – CONSORT flow diagram.

handed according to the Edinburgh Handedness Inventory (Oldfield, 1971). The trial excluded individuals with severe non-verbal cognitive deficits that often occur in the visual domain and may have caused problems in the testing or in the therapy sessions (cf. El Hachioui et al., 2014). Concerning visual short-term memory, our patient sample scored, on average, within the normal range on the Corsi Block-Tapping Task (Kessels, van Zandvoort, Postma, Kappelle, & de Haan, 2000). To prevent non-treatment effects related to spontaneous recovery of symptoms, patients were at least one year post-onset of disease at the time of initial testing (cf. Kertesz, 1984). The trial was registered prospectively (German Clinical Trials Register; identifier: DRKS00005482) and approved by the ethics review board at the Charité University Hospital in Berlin, Germany, with informed consent obtained from all patients.

Language abilities at baseline were assessed using a standardized aphasia test battery, the Aachen Aphasia Test (AAT; Huber, Poeck, & Willmes, 1984). The neurological diagnosis of aphasia was confirmed in all individuals, with one exception (patient 02), as indicated by the AAT Token Test (cf. Orgass & Poeck, 1966). Therefore, primary data analysis focused on the 17 individuals with confirmed aphasia, while further evaluations addressed the entire group of 18 persons. Structural T_1-weighted magnetic resonance imaging was performed for all patients using a 3T Magnetom Trio scanner (Siemens Medical Solutions, Erlangen, Germany). Sixteen patients had suffered a single cerebrovascular accident with subsequent lesions in parts of the left frontal, parietal, and temporal lobes, as well as in adjacent subcortical areas. The sample included two additional persons with left-hemisphere lesions resulting from traumatic brain injury (patient 03) and viral encephalopathy (patient 15). Lesions in both of these persons were most prominent in left perisylvian and adjacent subcortical areas. Two clinical neuroscientists manually delineated and superimposed the precise locations of lesioned voxels in all patients using the software MRIcron (Rorden & Brett, 2000; for lesion overlay maps, see Fig. 2; for individual case histories and baseline test scores, see Tables 1 and 2).

2.2. Study design and randomization

In a crossover design, patients were randomly assigned to one of two treatment orders: patients receiving ILAT prior to Naming Therapy (Group I; $n = 9$), and vice versa (Group II; $n = 9$). The group allocation was consistent with a previously determined computer-generated series of random numbers (0 or 1) and executed by an individual who alone had access to this list. Importantly, the individual did not participate in any stage of recruiting, screening, consenting, therapy or testing. According to Mann–Whitney U tests, the randomization procedure did not lead to significant differences between Group I and Group II with regard to: age, education level, months after onset of disease, individual lesion size, non-verbal short-term memory, and weekly hours of SLT before inclusion in the study. Crucially, any such differences were also absent on the mean AAT scores at baseline [$z = .58$, $p = .61$, not significant (n.s.)]. Moreover, the treatment groups were comparable in terms of gender and clinical diagnoses (for group averages and standard deviations, see Tables 1 and 2). Since patients with aphasia usually suffer from concomitant deficits in motor planning, it is worth noting that Group I and Group II were similarly affected by apraxia of speech, as diagnosed by two clinical linguists.

2.3. Treatment protocols and materials

ILAT was shaped according to everyday request communication and related social interaction (cf. Difrancesco et al., 2012). Three patients and a therapist were seated around a table and

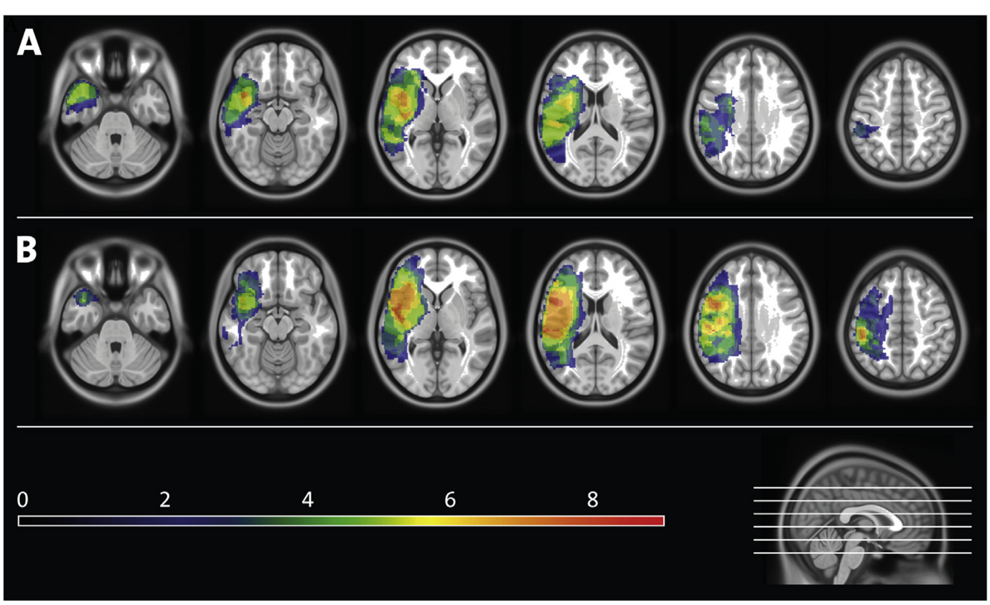

Fig. 2 – Lesion overlay maps. Patients received Intensive Language-Action Therapy prior to Naming Therapy (Group I; see Panel A), or vice versa (Group II; see Panel B). Different colors indicate the number of lesion overlaps in each treatment group.

Table 1 – Patient histories.

Patient	Gender	Age (in years)	Education level (in years)	Months after onset of disease	Origin
01	Male	49	13	41	Left MCA ischemia
02	Male	63	16	45	Left MCA ischemia
03	Female	45	21	49	Left perisylvian TBI
04	Female	41	18	97	Left MCA ischemia
05	Male	49	14	52	Left MCA ischemia
06	Male	54	21	49	Left MCA ischemia
07	Female	35	12	13	Left MCA ischemia
08	Male	32	14	40	Left MCA ischemia
09	Male	62	17	23	Left MCA ischemia
Group I					
Mean (SD)		**47.8 (10.2)**	**16.2 (3.1)**	**45.4 (21.9)**	
10	Male	73	19	61	Left MCA ischemia
11	Female	39	12	78	Left MCA ischemia
12	Female	49	13	149	Left MCA ischemia
13	Male	51	12	42	Left MCA ischemia
14	Male	63	13	31	Left MCA ischemia
15	Male	66	13	77	Left perisylvian VE
16	Female	47	12	245	Left MCA ischemia
17	Female	37	11	30	Left MCA ischemia
18	Male	65	25	239	Left MCA ischemia
Group II					
Mean (SD)		**54.4 (12.0)**	**14.4 (4.3)**	**105.8 (80.3)**	

Patients are listed according to treatment order: Group I (ILAT; Naming Therapy), and Group II (Naming Therapy; ILAT).
MCA = Middle cerebral artery; TBI = Traumatic brain injury; VE = Viral encephalopathy; SD = Standard deviation.

Table 2 – Baseline test scores.

Patient	Token Test	Repetition	Naming	Comprehension	CBTT	Neurological diagnosis
01	37	48	48	47	4	Moderate-severe Broca's aphasia
02	66	62	59	61	6	Mild Broca's aphasia
03	42	57	41	44	3	Moderate-severe global aphasia
04	51	59	53	70	6	Moderate Broca's aphasia
05	51	61	53	64	7	Moderate Broca's aphasia
06	48	45	56	62	6	Moderate Broca's aphasia
07	33	37	39	47	7	Severe Broca's aphasia
08	56	54	57	78	7	Mild Broca's aphasia
09	42	43	39	47	5	Severe global aphasia
Group I						
Mean (SD)	**47.3 (9.5)**	**51.8 (8.4)**	**49.4 (7.5)**	**57.8 (11.4)**	**5.7 (1.3)**	
10	41	42	41	34	3	Severe global aphasia
11	44	46	47	45	6	Moderate Broca's aphasia
12	48	48	48	53	4	Moderate Broca's aphasia
13	51	45	49	49	6	Moderate Broca's aphasia
14	54	52	49	48	6	Moderate Broca's aphasia
15	33	43	39	46	3	Severe global aphasia
16	55	59	68	62	6	Mild Broca's aphasia
17	54	53	53	57	6	Mild-moderate Broca's aphasia
18	47	52	46	49	6	Moderate Broca's aphasia
Group II						
Mean (SD)	**47.4 (6.8)**	**48.9 (5.2)**	**48.9 (7.9)**	**49.2 (7.5)**	**5.1 (1.3)**	

Individual *t*-scores obtained on the Aachen Aphasia Test. Token Test: severe (0–43), moderate (44–53), light (54–62) or mild disorder (≥63). Repetition: severe (0–43), moderate (44–53), light (54–62) or mild disorder (≥63). Naming: severe (0–43), moderate (44–53), light (54–62) or mild disorder (≥63). Comprehension: severe (0–43), moderate (44–53), light (54–63) or mild disorder (≥64). Non-verbal short-term memory was assessed using the Corsi Block-Tapping Task. All scores and means are shown separately for Group I (ILAT; Naming Therapy), and Group II (Naming Therapy; ILAT).
CBTT = Corsi Block-Tapping Task; SD = Standard deviation.

provided with picture cards showing different objects. Each card had a duplicate that was owned by one of the other players. Barriers on the table prevented players from seeing each others' cards. The goal was to obtain a pair of identical cards by verbally requesting the duplicate from a fellow player. Request utterances included the name of an object embedded in a carrier phrase [e.g., “I want the (...),” “Could I please have the (...)”]. If the duplicate was available, the players compared the depicted objects and, in the case of a match, the addressee handed over the corresponding card to the requesting person. If the duplicate was not available, the addressee rejected the request. In the event of misunderstandings, the players asked clarifying questions. This rich action-sequence structure encouraged the use of formulaic expressions (e.g., "Here you are," "Thank you," "You're welcome"; cf. Stahl & Van Lancker Sidtis, 2015). The complexity of the communicative interaction was tailored to the patients' individual language skills by varying the difficulty level of the target words and the carrier phrases.

Naming Therapy was conceived to resemble ILAT in as many ways as possible, except for the fact that the players did not use verbal utterances for communication and social interaction. Instead, the goal was to name or describe objects shown on the picture cards. Three patients and a therapist were seated around the table, on which cards were placed exactly as during ILAT, but with the barriers removed. The players took turns in clockwise order, picking a card from their own set and finding an appropriate designation for the depicted object. The name of an object was embedded in a carrier phrase of similar length and syntactic complexity as during ILAT [e.g., "This is a (…)," "Here I can see a (…)"]. Patients were able to observe whether or not other players identified an object correctly. Again, the difficulty level of the target words and the carrier phrases was tailored to the patients' individual language skills. Critically, the total number of verbal utterances did not differ between ILAT and Naming Therapy.

In both types of training, the therapist (i) acted as a model by using individual carrier phrases, (ii) provided instruction and advice (cueing strategies, etc.) whenever helpful, and (iii) motivated participants by giving positive feedback. The training materials were designed for the purpose of the current trial. Each set of cards included 12 picture pairs. For tailoring these sets to individual language skills, the following difficulty levels were available: items with high ($n = 48$ different pictures), medium ($n = 48$), and low ($n = 48$) normalized lemma frequency; phonological minimal pairs ($n = 96$); and items from only one semantic category ($n = 48$). Card sets of one difficulty level were matched for mean normalized lemma frequency to ensure that items of each category were similarly challenging. All 24 card sets were split into two packets with equal numbers of items per difficulty level and assigned to ILAT or Naming Therapy in counterbalanced order across treatment groups.

2.4. *Clinical procedure*

Recruitment, screening and training sessions took place at an outpatient rehabilitation center located in Berlin, Germany. The training was delivered by an experienced clinical neuroscientist serving as a therapist. Groups of three patients who were relatively heterogeneous with regard to symptom severity underwent ILAT and Naming Therapy in the order determined by the randomization procedure described above. The schedule included a 6-day recreation interval between the two treatments (see Fig. 3). Both types of training were administered with the same high intensity (3.5 h per session with short breaks, if necessary) and duration (six consecutive working days), resulting in overall 42 h of treatment within less than four weeks. Patients completed all training sessions with no signs of fatigue and did not attend any other form of SLT throughout the entire trial (cf. Hoffmann et al., 2014).

A clinical neuropsychologist tested each patient one day before (T_1) and one day after the first training period (T_2), as well as one day after the second training period (T_3). The neuropsychologist was blinded to the group assignment and did not have patient contact apart from the testing sessions. Changes in language abilities were assessed using a standardized aphasia test battery, known for its good re-test reliability (AAT; Huber et al., 1984). Language performance was measured on four subscales of the battery: Token Test, Repetition, Naming, and Comprehension. AAT results were designated as normally distributed *t*-scores, averaged across subscales. These mean AAT scores served as *primary* outcome measure to investigate changes in general language performance over time. As both types of training focused on verbal expression in individuals with non-fluent aphasia, scores on the combined AAT subscales requiring speech production—Naming and Repetition—were considered as a *second* measure of interest.

2.5. *Statistical analysis*

Statistical evaluations indicated negligible carryover effects in our crossover design, suggesting interpretable data in both training periods [$t(16) = -1.54$, $p = .15$, n.s.; for details, see Jones & Kenward, 2002]. Repeated-measures analyses of variance (ANOVAs) were conducted, including within-subject factor Time (T_1; T_2; T_3) and between-subject factor Group (Group I; Group II), with two-tailed *p* values and alpha levels of .05 applied for all statistical tests.

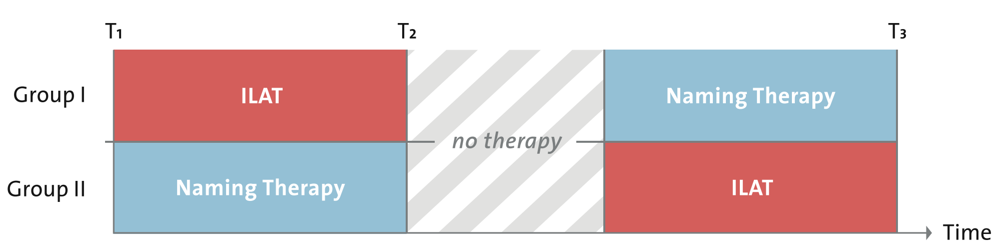

Fig. 3 – Study design. Group I received Intensive Language-Action Therapy (ILAT) prior to Naming Therapy, while Group II attended both types of training in reverse order. Patients underwent testing before treatment onset (T_1), after the first treatment (T_2), and after the second treatment (T_3).

3. Results

A repeated-measures ANOVA revealed a significant interaction of Time and Group based on the mean AAT scores [$F(2, 30) = 6.91$, $p = .003$, $\eta^2 = .12$]. This complex interaction was explored in subsequent ANOVA contrasts. In the *first* training period, ILAT yielded better outcomes than Naming Therapy [Time × Group interaction between T_1 and T_2: $F(1, 15) = 4.72$, $p = .046$, $\eta^2 = .08$]. In the *second* training period, this differential pattern of results was even more pronounced [Time × Group interaction between T_2 and T_3: $F(1, 15) = 15.85$, $p = .001$, $\eta^2 = .41$; see Fig. 4A and Table 3A].

The ANOVA focusing on mean AAT production scores revealed a significant interaction of Time and Group [$F(2, 30) = 5.48$, $p = .009$, $\eta^2 = .14$]. Subsequent exploratory ANOVA contrasts indicated a superiority of ILAT over Naming Therapy in the *first* training period [Time × Group interaction between T_1 and T_2: $F(1, 15) = 5.87$, $p = .03$, $\eta^2 = .21$] and in the *second* training period [Time × Group interaction between T_2 and T_3: $F(1, 15) = 10.43$, $p = .006$, $\eta^2 = .53$; see Fig. 4B and Table 3A].

Comparing the mean AAT scores from *both* training periods before and after each type of intervention in *post-hoc* evaluations, the ANOVA suggested significant progress in language performance with ILAT [main effect of Time: $F(1, 15) = 108.24$, $p < .001$, $\eta^2 = .87$], independent of whether the treatment had been applied initially or in second position [Time × Group interaction: $F(1, 15) = .55$, n.s.]. Naming Therapy did not consistently lead to progress in language performance [main effect of Time: $F(1, 15) = 1.46$, n.s.], but this treatment was relatively more effective initially than in

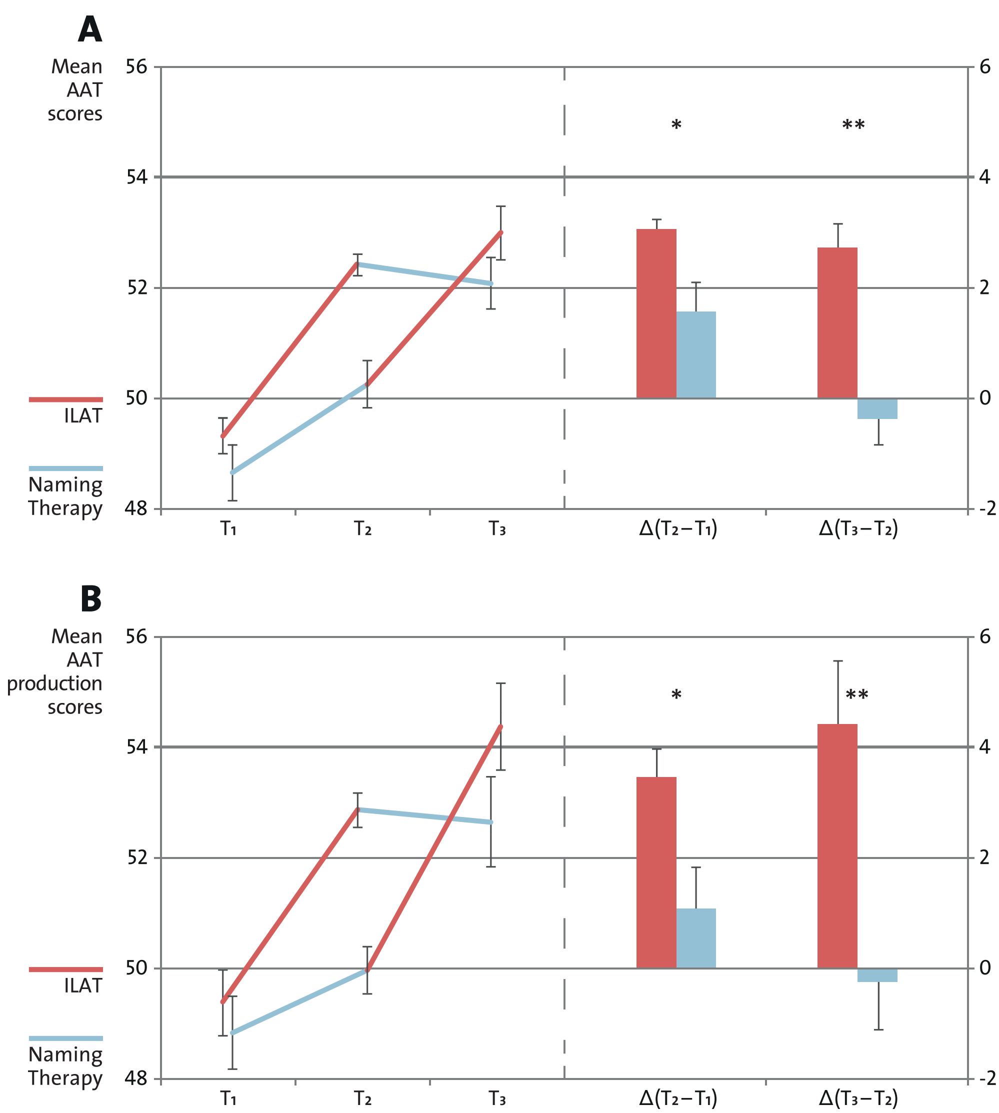

Fig. 4 – Aphasia test results. Changes in language performance on the Aachen Aphasia Test (AAT), based on mean scores across all subscales (Panel A) and speech production measures only (Panel B). Individuals with chronic aphasia were randomly assigned to one of two Groups: Intensive Language-Action Therapy (ILAT) administered prior to Naming Therapy, or vice versa. Patients were tested at three points in Time: before treatment onset (T_1), after the first treatment (T_2), and after the second treatment (T_3). AAT results indicate significant interactions of Time and Group in the *first* training period [$\Delta(T_2-T_1)$] and in the *second* training period [$\Delta(T_3-T_2)$], as revealed by repeated-measures analyses of variance (*$p < .05$; **$p < .01$).

Table 3 – Aphasia test results.

A. Group averages for all patients with confirmed aphasia					
Mean AAT scores	T_1	T_2	T_3	$\Delta(T_2-T_1)$	$\Delta(T_3-T_2)$
Group I (SD)	49.4 (9.4)	52.5 (9.5)	52.1 (10.8)	3.1 (.5)*	−.4 (1.7)
Group II (SD)	48.7 (6.7)	50.3 (7.0)	52.9 (7.5)	1.5 (2.0)	2.7 (1.5)*
Mean AAT production scores	T_1	T_2	T_3	$\Delta(T_2-T_1)$	$\Delta(T_3-T_2)$
Group I (SD)	49.4 (7.0)	52.8 (8.0)	52.6 (9.9)	3.4 (1.6)*	−.3 (2.8)
Group II (SD)	48.9 (6.7)	49.9 (5.6)	54.4 (7.6)	1.1 (2.3)	4.4 (3.2)**
B. Group averages for all patients, including one individual without confirmed aphasia					
Mean AAT scores	T_1	T_2	T_3	$\Delta(T_2-T_1)$	$\Delta(T_3-T_2)$
Group I (SD)	50.8 (9.7)	53.8 (9.6)	53.2 (10.6)	2.9 (.7)**	−.6 (1.7)
Group II (SD)	48.7 (6.7)	50.3 (7.0)	52.9 (7.5)	1.5 (2.0)	2.7 (1.5)*
Mean AAT production scores	T_1	T_2	T_3	$\Delta(T_2-T_1)$	$\Delta(T_3-T_2)$
Group I (SD)	50.6 (7.5)	54.1 (8.4)	53.5 (9.7)	3.4 (1.5)**	−.6 (2.7)
Group II (SD)	48.9 (6.7)	49.9 (5.6)	54.4 (7.6)	1.1 (2.3)	4.4 (3.2)**

Aachen Aphasia Test (AAT) results averaged across all subscales (Mean AAT scores) and subscales requiring speech production (Mean AAT production scores). Individuals with chronic aphasia were randomly assigned to one of two treatment groups: patients receiving Intensive Language-Action Therapy prior to Naming Therapy (Group I), or vice versa (Group II). Testing was administered at three points in time: before treatment (T_1), after the first treatment (T_2), and after the second treatment (T_3). Wilcoxon signed-rank tests revealed significantly increased aphasia test scores with ILAT (*$p < .05$; **$p < .01$) in the *first* training period [$\Delta(T_2-T_1)$] and in the *second* training period [$\Delta(T_3-T_2)$] for all patients with confirmed aphasia (Panel A) and after including one person who did not meet the criteria for diagnosis of aphasia according to the AAT Token Test (Panel B).
SD = Standard deviation.

second position [Time × Group interaction: $F(1, 15) = 4.55$, $p = .049$, $\eta^2 = .22$].

Further *post-hoc* analyses demonstrated the statistical significance of any finding reported here after including one individual who did not meet the criteria for diagnosis of aphasia according to the AAT Token Test [patient 02; see Table 3B]. In particular, the ANOVA confirmed the significant interaction of Time and Group on the mean AAT scores when considering the entire sample of 18 persons [$F(2, 32) = 7.95$, $p = .002$, $\eta^2 = .14$]. Likewise, excluding the two patients with aphasia following traumatic brain injury (patient 03) and viral encephalopathy (patient 15) did not alter the significant interaction of Time and Group [$F(2, 26) = 4.88$, $p = .02$, $\eta^2 = .09$].

4. Discussion

The present crossover RCT aimed to determine whether or not embedding language in the context of communication and social interaction increases the efficacy of intensive aphasia therapy. Individuals with chronic non-fluent aphasia each received two types of intensive training in counterbalanced order: communicative-pragmatic action-embedded therapy focusing on verbal requests (ILAT), and utterance-centered confrontation naming (Naming Therapy). Both types of training were delivered with the same high intensity and duration, with therapy materials and number of utterances matched between treatment groups. Scores on a standardized aphasia test battery revealed significant progress in language performance with ILAT, independent of when this method was administered. In contrast, Naming Therapy failed to produce significant progress in language performance, leading to a positive trend only at the onset of the treatment, but not when applied after previous intensive training. Notably, treatment type explained 41 percent of the variance associated with changes in language performance in the later training period. This strong effect is consistent with the observation that our data indicated similar patterns of individual changes in aphasia test scores, irrespective of symptom severity. Increases in aphasia test scores were most prominent on speech production measures, possibly reflecting the fact that both types of training focused on spoken language in individuals with prevailing expressive deficits. The current results demonstrate the overall efficacy of communicative-pragmatic action-embedded therapy in chronic non-fluent aphasia, whereas any benefit from utterance-centered object naming appears to be limited to the early training period. Future research will be required to substantiate these findings with regard to generalization to discourse in everyday life.

We wish to emphasize that all of our patients signed up to the intensive SLT with great expectations, hoping for better outcomes relative to the standard treatment available in Germany, which rarely amounts to more than 3 h of training per week. Consequently, progress in language performance observed during the early training phase might be interpreted as a non-specific placebo effect. It should be pointed out, however, that the superiority of ILAT over Naming Therapy in this early training phase reached statistical significance (manifest as an interaction of Time and Group on aphasia test scores; ANOVA contrast: $p = .046$). The superiority of ILAT over Naming Therapy was most apparent on the *a priori* motivated speech production measures (ANOVA contrast: $p = .03$). Although we acknowledge the slightly increased risk of false-positive results arising from multiple comparisons in our dataset, these findings rule out the possibility that a non-specific effect explains all changes in the initial training period.

A number of clinical trials indicate that improved scores on standardized aphasia tests remain stable in the weeks and months following ILAT (Berthier et al., 2009; Meinzer et al., 2005) and intensive regimes including utterance-centered object naming (Berthier et al., 2014; Rose, Attard, Mok, Lanyon, & Foster, 2013). Hence, progress in language performance observed during the second training period is unlikely to result from the preceding treatment, regardless of whether patients had previously received ILAT or Naming Therapy. Statistical evaluations lend support to this claim, suggesting uncontaminated data in the second training period (cf. Jones & Kenward, 2002). However, we appreciate that statistical evaluations cannot guarantee the absence of carryover effects in crossover designs. We therefore recommend interpreting data from the final phase of the treatment with caution, whereas the superiority of ILAT over Naming Therapy in the early training period should be robust to such criticism.

The randomization procedure applied proved to be successful, as statistical analyses did not reveal between-group differences before therapy on any of our variables assessed (see section Methods). However, it was inevitable to find non-significant numerical differences in group averages. Group I tended towards higher education levels and elevated aphasia test scores at baseline that, arguably, may bear the danger of ceiling effects. In contrast, Group II tended to have older age and longer time after onset of disease, possibly putting these patients in a slight disadvantage. We wish to highlight that such numerical differences were mostly due to single outlier values in persons who otherwise showed treatment-related changes in language performance consistent with the remaining patient sample. Moreover, including one individual who did not meet the criteria for diagnosis of aphasia did not affect any finding reported here (see section Results). Crucially, the treatment groups appear to be well matched according to the baseline scores on the AAT Token Test (averages: 47.3 *vs* 47.4; see Table 2), an outcome measure known to reflect the severity level of aphasia (cf. Huber et al., 1984). Overall, these results do not provide evidence of systematic between-group differences that may limit the interpretation of our data.

The current patient sample included 15 persons with chronic aphasia following a left-hemisphere cerebrovascular accident. Our data replicate the finding that ILAT is a relatively effective treatment of chronic post-stroke aphasia, as demonstrated by earlier RCTs (Meinzer et al., 2005; Pulvermüller et al., 2001; Szaflarski et al., 2015) and further well designed studies (Barthel, Meinzer, & Djundja, 2008; Kurland, Pulvermüller, Silva, Burke, & Andrianopoulos, 2012; Maher et al., 2006; Rose et al., 2013). In addition to persons with vascular aetiologies, our patient sample included two individuals with chronic aphasia following traumatic brain injury and viral encephalopathy. We wish to point out that statistical analyses without these two individuals fully confirmed any group result. Moreover, the two individuals showed numerical increases in aphasia test scores consistent with patients suffering from chronic post-stroke aphasia. Future trials will be needed to clarify whether or not benefits from ILAT can be extended to patients with chronic aphasia of non-vascular origin.

The most important question opened by the present crossover RCT addresses the underlying reasons for the superiority of ILAT over Naming Therapy, yet without challenging the efficacy of traditional utterance-centered approaches as such (cf. Howard, Patterson, Franklin, Orchard-Lisle, & Morton, 1985). Many factors are unlikely to account for our differential outcome, as our design controlled for the influence of training intensity and duration, treatment order, the clinical setting in patient groups, as well as the number of utterances. Guided by neuroscience research, we submit that the rich action-sequence structure of ILAT was essential for its overall success. Three more specific sub-aspects of this action-sequence structure deserve closer attention, as each of them offers a separate view on the potential neural mechanisms of speech and language recovery after stroke.

(I) With a request performed during ILAT, players are able to predict a set of possible partner actions. For example, players may anticipate whether or not the conversation partner accepts a request and hands over the corresponding picture card. Neuroscience evidence suggests that the prediction of such linguistic and non-linguistic action sequences involves the cortical motor system (Carota et al., 2010). Further evidence indicates that engagement of the cortical motor system can be causal for language processing in left perisylvian eloquent areas (Schomers, Kirilina, Weigand, Bajbouj, & Pulvermüller, 2015). Given that at least part of the motor system was intact in all of our patients, activity in these neural circuits may have supported linguistic representations in left perilesional language networks (Pulvermüller & Fadiga, 2010). In contrast to ILAT, Naming Therapy does not provide a similarly rich action-sequence structure. The superiority of ILAT in the current trial may thus result from the fact that this type of training was more effective in exploiting the neural bases of action-sequence prediction in the cortical motor system (Berthier & Pulvermüller, 2011).

(II) A similar point touches on other neural mechanisms underpinning higher cognitive functions relevant for communication and social interaction. For example, the prediction of action sequences in ILAT entails “common ground” between players, including assumptions about intentions and strategies of the conversation partner. Neuroscience evidence suggests that the range of skills necessary to attribute mental states to other persons, known as “theory of mind,” depends on bilateral prefrontal and temporoparietal areas, part of which were intact in our patients (Sebastian et al., 2012). As features related to common ground are less prominent in Naming Therapy, one further reason for the general efficacy of ILAT may emerge from potential synergies between left perisylvian eloquent areas and neural circuits associated with theory of mind processing. Previous studies indeed confirm that cortical language (Broca's area) and motor regions (precentral gyrus) are more strongly involved during requesting—the critical speech act in our ILAT protocol—than during naming (Egorova et al., 2013, 2014, 2016). Still, future research will be required to delineate the precise neuroplastic changes carrying distinct outcomes of ILAT (e.g., Barbancho et al., 2015; Meinzer et al., 2004; Mohr et al., 2016).

(III) Consistent with patterns of communicative interaction frequently observed in everyday life, the rich action-sequence structure of ILAT encourages the use of formulaic expressions (cf. Stahl & Van Lancker Sidtis, 2015). Depending on the availability of picture cards, players interact with sets of formulaic expressions to indicate whether a request was accepted ("Here you are," "Thank you," "You're welcome"), rejected ("I'm sorry," "No problem," "Too bad") or unclear ("Pardon me?"). Neuroscience evidence suggests that this linguistic category of utterances engages, in particular, right-hemisphere cortical and bilateral subcortical areas (e.g., Sidtis, Canterucci, & Katsnelson, 2009; Speedie, Wertman, Ta'ir, & Heilman, 1993; Van Lancker Sidtis & Postman, 2006). As a result, formulaic expressions are often preserved in aphasic speech and may be viewed as a valuable motivational resource in therapy, especially in severely affected patients (Stahl, Kotz, Henseler, Turner, & Geyer, 2011). To compensate for the higher proportion of formulaic expressions in ILAT, the amount of non-formulaic target-related words and sentences tended to be larger in Naming Therapy, thus balancing the total number of utterances between the two types of training. Therefore, an additional potential strength of ILAT may arise from its communicative-pragmatic nature that enables patients to tap into neural resources supporting formulaic expressions.

This is the first RCT that provides direct clinical evidence for the impact of communicative language function on recovery from chronic non-fluent aphasia. Our results demonstrate that using language as a tool for communication and social interaction makes intensive aphasia therapy more effective. In contrast, the strategy to focus on utterances *per se* seems to be less effective, at least in the current non-communicative context of confrontation naming. This finding casts doubt on a once common view in aphasia rehabilitation, according to which utterance-centered approaches are necessary to facilitate word and sentence processing before communicative-pragmatic SLT can be successful. In conclusion, it appears that the damaged left perisylvian language system of the human brain benefits most when linguistic forms are practiced in communicative interaction.

Acknowledgments

Above all, we wish to thank our patients for engaging in the daily therapy sessions, along with our motivated students Adriana Gießler, James Kerr, and Melina Riegel. We also wish to thank Sebastian Kaim, Dr Cora Kim, and Laura Schiemann for helping us create our comprehensive card sets. Finally, we are grateful to the team at our Berlin host clinic Zentrum für ambulante Rehabilitation—Julia Funk, Anne Gengenbach, Karin Lohmann, Anke Nicklas, Dorothee Sydow, and Prof. Diethard Steube—for making this work possible. The current trial was supported by the Deutsche Forschungsgemeinschaft (Pu 97/15-1 to FP) and the Deutsche Akademische Austauschdienst (fellowship to GL) in the absence of competing financial interests.

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