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RESEARCH ARTICLE

Inter-brain plasticity as a mechanism of change in psychotherapy: A proof of concept focusing on test anxiety

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Abstract
Objective.: There is a growing consensus that interpersonal processes are key to understanding psychotherapy. How might that be reflected in the brain? Recent research proposes that inter-brain synchrony is a crucial neural component of interpersonal interaction. The current proof-of-concept study examines, for the first time, therapist-patient inter-brain synchrony measurement during multiple sessions. To guide the design of future studies, we performed a precursory test in a small sample of the association between inter-brain synchrony and therapeutic change, hypothesizing that it would gradually increase over therapy, reflecting inter-brain plasticity.
Method.: We scanned 18 therapy sessions of participants ($N = 8$) who underwent a 6-session test anxiety treatment. We measured therapist and patient brain activity using functional near-infrared spectroscopy (fNIRS) and assessed perceived session quality, wellbeing, symptoms, and therapeutic alliance every session.
Results.: In this proof-of-concept sample inter-brain synchrony gradually increased over treatment, and was associated with reduced symptoms, improved wellbeing and perceived session quality, but not with a stronger therapeutic alliance. fNIRS imaging had no discernable adverse effects.
Conclusion.: Our findings demonstrate that fNIRS imaging during psychotherapy is a feasible and viable research method and that inter-brain plasticity should be a candidate for future research on biological mechanisms underlying therapeutic change.

Keywords: neuroimaging; synchrony; test anxiety; psychotherapy

Clinical or methodological significance of this article: Previous research has linked inter-brain synchrony—coordinated activity in two people's brains—to better interpersonal relationships. The current study provides a proof of concept for measuring inter-brain synchrony between patients and therapists during multi-session psychotherapy, showing that it increases over time and is correlated with symptom reduction. This small scale examination provides initial evidence that inter-brain plasticity—lasting change in inter-brain synchrony—may go along with therapeutic change.

Extensive research increasingly recognizes the critical importance of understanding the patient-therapist relationship (i.e., the therapeutic alliance) in predicting the changes that occur during psychotherapy (Doran, 2016; Flückiger et al., 2018). This is reinforced by the majority of theoretical approaches in psychotherapy, which emphasize the pivotal role of interpersonal relationships in therapy (Blagys & Hilsenroth, 2000; Hopwood et al., 2021; Mitchell & Aron, 1999; Stolorow et al., 2014). In

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line with these theories, the therapeutic relationship emerges as a robust predictor of treatment effectiveness across diverse therapeutic methodologies and mental health interventions (Flückiger et al., 2018; Totura et al., 2018).

One particularly promising area of research within the context of the patient-therapist interaction is the examination of interpersonal synchrony (Koole et al., 2020). Interpersonal synchrony, the coordination of simultaneous physical behavior between two or more people, may represent higher levels of emotional connection (Hove & Risen, 2009) which is critical for the therapist-client relationship. Synchrony can increase sense of cohesion (Shamay-Tsoory et al., 2019), the ability to learn from others (Pärnamets et al., 2020), and improves predictions about others (Miles et al., 2009), thereby conserving cognitive resources for other tasks (Hoehl et al., 2021).

Various methodologies have been employed to assess different aspects of synchrony between patients and therapists within the psychotherapy framework. These methods include evaluations of motor synchrony (e.g., Ramseyer & Tschacher, 2011), electrodermal activity synchrony (Bar-Kalifa et al., 2019), heart rate (e.g., Tschacher & Meier, 2020), and the synchronization of oxytocin neurohormone release (e.g., Zilcha-Mano et al., 2021). Behavioral synchrony, encompassing aspects such as motion, voice, and language, has already demonstrated its association with improved outcomes (Koole et al., 2020; Wiltshire et al., 2020).

One type of therapist-patient synchrony which has rarely been examined is inter-brain synchrony—i.e., synchrony between therapists' and patients' brain activity. This phenomenon is thought to arise from the exchange of signals between brains through external means, such as speech, gestures, and facial expressions (Hasson et al., 2012). Through this exchange in signals, activity in each brain becomes correlated with activity in the other brain, facilitating their ability to mutually predict each other's states ultimately enhancing aligned, cooperative behavior. As such, this mechanism might underlie behavioral synchrony and interpersonal connection in general. Evidence from hyperscanning functional near-infrared spectroscopy (fNIRS) studies consistently highlights the role of inter-brain synchrony, particularly within the inferior frontal gyrus (IFG), in social alignment. The IFG, along with the inferior parietal lobule (IPL) and premotor (PM) cortices, constitutes the observation-execution system (Rizzolatti & Sinigaglia, 2016). Studies have shown increased inter-brain synchrony in the IFG during face-to-face dialogues (Jiang et al., 2012), movement synchronization (Marton-Alper et al., 2023) and synchronized song learning predicts task performance (Pan et al., 2018). Non-psychotherapy studies have connected inter-brain synchrony with positive interaction outcomes (Czeszumski et al., 2022), and a study on inter-brain synchrony in single-session consultations found it to be higher in counseling than in casual conversation, and to be associated with a stronger therapeutic alliance (Zhang et al., 2018).

Notably, the inter-brain plasticity in psychotherapy model (Sened et al., 2022) suggests that not only is therapy associated with *high* synchrony, we should also expect it to be associated with *increases* in inter-brain synchrony. A variety of conditions linked to difficulties in interpersonal interaction are associated with reduced inter-brain synchrony (e.g., borderline personality disorder, Bilek et al., 2017; or autism, Georgescu et al., 2020; Kaur et al., 2018). As therapy addresses some of these issues, we should expect a matching increase in inter-brain synchrony. One study supporting this idea showed that patients with borderline personality disorder in remission had higher inter-brain synchrony compared to patients with an active condition (Bilek et al., 2017), suggesting that whichever processes led to remission (the study did not specifically examine whether remission was due to therapy) have also led to increases in inter-brain synchrony. Other studies have shown more directly that behavioral synchrony, which is associated with inter-brain synchrony (Dumas et al., 2010; Novembre et al., 2017), increases over the course of therapy (Galbusera et al., 2018; Venuti et al., 2017).

Inter-brain plasticity theory (Shamay-Tsoory, 2021) provides a biological mechanism through which this increase might happen. Inter-brain plasticity is an expansion of well-established mechanisms for *intra*-brain plasticity—i.e., long-term changes in connectivity between neurons in a single brain. One of the main mechanisms for intra-brain plasticity is Spike-Timing Dependent Plasticity (STDP; Caporale & Dan, 2008)—the consistent finding that when two neurons fire in close succession, the connection between them grows stronger. Inter-brain plasticity proposes that when two neurons in different people's brain fire in close succession due to communication between them, the connection between those neurons will also grow stronger. This does not require any new biological mechanism beyond STDP. Rather, it stems from the fact that during a communication act (e.g., saying a sentence to the other person), regions associated with an inner mental state are activated simultaneously with regions associated with communication production (e.g., moving the mouth to form words) in the communication initiator's brain; this

activation is associated with activation of regions associated with perception in the communication receiver's brain, which are finally also associated with activation of inner mental states in the receiver (Zada et al., 2024). According to STDP, this process should strengthen the connection between inner mental states and communication production in the initiator's brain, and between perception and inner mental states in the receiver's brain. Assuming that the receiver's perceptive abilities stay the same, or at least do not degrade, this should lead, transitively, to a stronger coordination of activity between inner mental state neurons in both brains. Thus, according to inter-brain plasticity theory, any situation in which people experience high inter-brain synchrony should lead, over time, to a long-term increase in synchrony.

If therapy is such a situation with high inter-brain synchrony, it might contribute to the patient's capability for synchrony, which might, in turn, improve their interpersonal interactions and be part of a general amelioration in their condition. As the therapist consistently exhibits empathic and attuned behavior, inter-brain synchrony strengthens. This leads to increased inter-brain synchrony with the therapist that persists between sessions, and might ultimately lead to improved inter-brain synchrony outside of therapy—reflected behaviorally by improved interpersonal interactions and improved wellbeing (see Figure 1). Thus, inter-brain plasticity might underlie some benefits of psychotherapy.

To examine these hypotheses, or any other hypothesis regarding changes in therapist-patient inter-brain synchrony over time, researchers must perform imaging of therapists and patients in actual, multi-session treatment. The current study is an initial foray into this field, going beyond a single consultation, to provide the first examination of inter-brain synchrony and plasticity over the course of actual treatment. Specifically, we used a functional near-infrared spectroscopy setup (fNIRS; Ferrari & Quaresima, 2012) to perform brain imaging in a traditional clinic setting, using special caps worn by both patient and therapist. Building on the role of the IFG in cognitive and emotional alignment (Shamay-Tsoory et al., 2019), we focused on inter-brain synchrony in this region. By examining brain activity during multiple psychotherapy sessions, we could test the following hypotheses which cannot be examined in a single session: (1) Inter-brain synchrony will increase during psychotherapy, i.e., inter-brain plasticity would occur (pre-registered), (2) This increase will generalize to synchrony with another person—namely, a clinical interviewer (pre-registered), and (3) The increase in synchrony will be related to therapeutic outcome (exploratory).

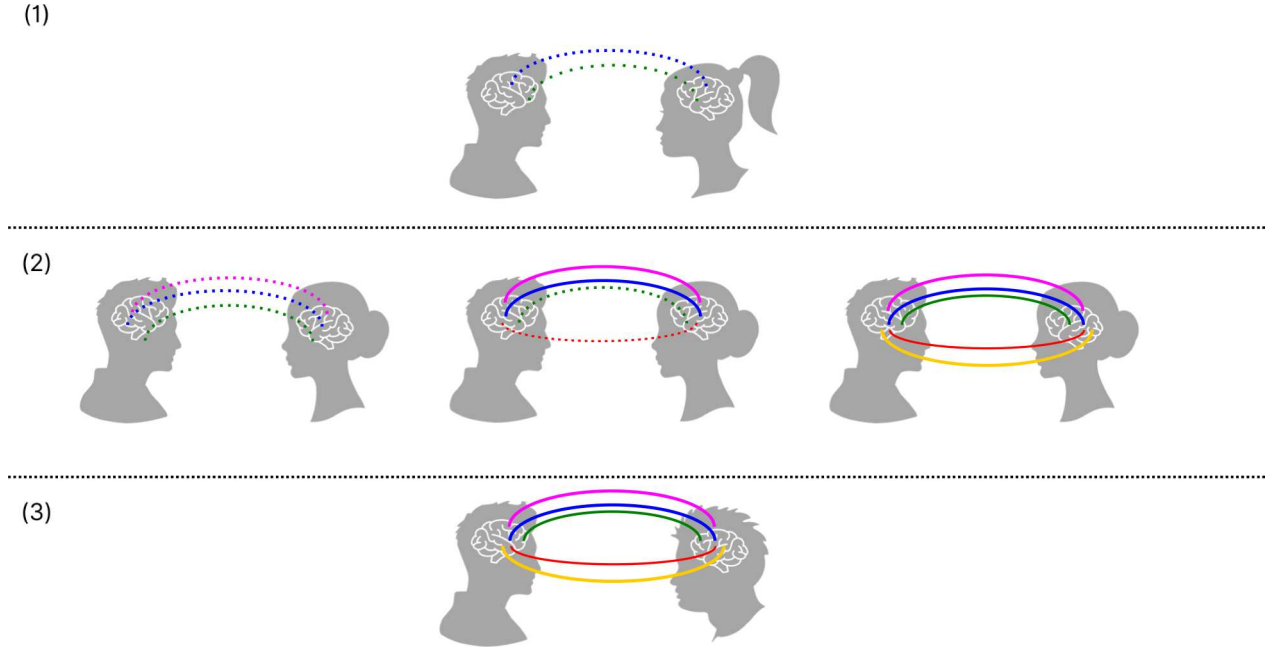

Figure 1. Therapy improving interpersonal interactions through inter-brain plasticity. According to the proposed model, (1) a patient (left) has interpersonal difficulties which manifest biologically as weak inter-brain synchrony. (2) The patient (left) goes through multiple sessions with a therapist (from left to right). Inter-brain synchrony gradually improves through inter-brain plasticity. (3) After therapy, the patient has better inter-brain synchrony when meeting a new person, reflecting better interpersonal interactions.

Method

The study was approved by the institutional IRB; study procedure and main hypotheses were registered on clinicaltrials.gov, identifier NCT05336734 after data collection ended but before analyses were conducted. We report how we determined our sample size, all data exclusions, all manipulations, and all measures in the study. (Sample size determination and measures unrelated to the current manuscript are detailed in the supplementary material). While the study was not designed or powered to show treatment efficacy, we report and briefly discuss treatment outcome results in the supplementary material. Full data and code are at https://osf.io/cepuf/?view_only = b4681f8f19e441f588542e3f58c4c605.

Participants

Participants were recruited through social media posts in student discussion groups. Eight participants—6 women and 2 men—came to an initial interview, all of whom met inclusion criteria and completed the entire study course (see full CONSORT flowchart in Figure 2). Seven participants were Jewish and 1 was Arab-Christian. Inclusion criteria were a Test Anxiety Inventory (TAI; Spielberger, 2010) score of at least 50, a value of 1 or less in the BDI-II suicide item, no current psychotherapy addressing test anxiety, and no comorbid disorders except for anxiety disorders and single-episode MDD (as assessed by the DIAMOND clinical interview; Tolin et al., 2018). Participants did not pay for therapy and received no other compensation.

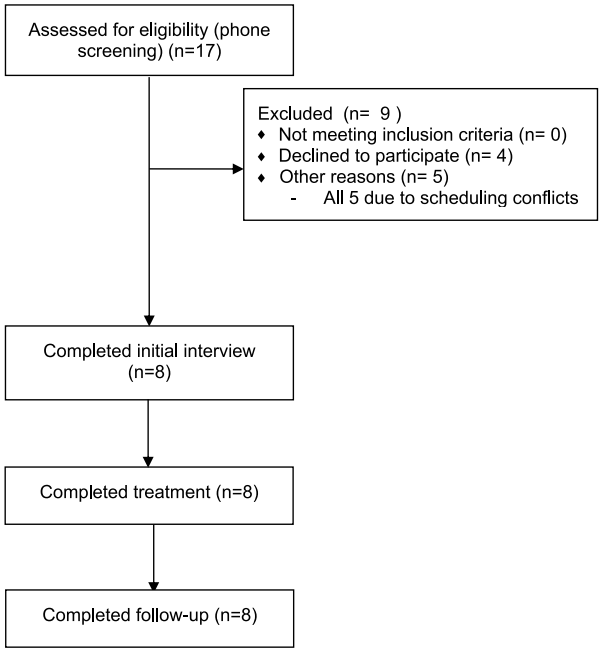

Figure 2. CONSORT diagram of treatment participation.

Sample size was determined by practical considerations - we aimed to recruit as many participants possible over a period of about 8 months in which study budget allowed for the therapist, supervisor, and equipment to treat 3 patients a week, aiming for 12 subjects. Due to the COVID-19 pandemic, local guidelines did not allow recruitment of new participants for parts of this period (existing treatments continued as usual), leading to a final sample size of 8 participants.

Procedure

The study consisted of a total of eight sessions per participant—a screening session, six therapy sessions, and a follow-up session. Participants who indicated interest in the study were sent an online questionnaire which included the TAI and the BDI-II. Participants who met criteria came to a baseline session. After signing a consent form, participants sat down with an interviewer who conducted a verbal interview consisting of the TAI, used as a structured interview, as well as the DIAMOND initial interview (a specific part of the DIAMOND), while both were connected to fNIRS. The devices were then disconnected, and the interviewer administered the rest of the DIAMOND. Participants also completed self-report measures.

One week later, participants began a therapy program for test anxiety consisting of 6 weekly sessions. Treatment involved imagery work and cognitive behavioral therapy, as described by Prinz et al. (2019; Full protocol at https://osf.io/uxn6m). On the first, third, and fifth treatment sessions, participants and therapists were connected to fNIRS devices for the duration of the session. Participants also completed self-report measures before and after the session.

In a follow-up session occurring one week later, participants met an unfamiliar interviewer who administered an interview identical to the first session interview; both were connected to fNIRS devices. Participants then completed self-report measures.

Therapists and Interviewers

Interviews were carried out by trained psychology students. Therapy sessions were conducted by the first author, who is a licensed clinical psychologist, supervised by a licensed clinical supervisor who has supervised multiple therapists administering the treatment protocol.

Table I. Descriptive statistics.

	N	Mean(SD)	Range	Reliability
Baseline Test Anxiety	8	64.5(10.41)	50–75	Cronbach's alpha = .89
Follow-up Test Anxiety	8	61.38(10.64)	44–72	Cronbach's alpha = .89
State Test Anxiety	44	27(5.01)	14–35	R_C = .77
Pre-session Wellbeing	44	254.86(89.06)	32–383	R_C = .81
Post-session Wellbeing	43	260.51(91.08)	44–390	R_C = .76
Therapeutic Alliance	43	29.95(5.2)	17–36	R_C = .66
Perceived Session Quality	43	22.77(2.67)	14–25	R_C = .7
Inter-brain Synchrony (Sessions)	18	.289(.019)	.252–.318	
Inter-brain Synchrony (Interviews)	12	.3(.017)	.278–.327	

Measures

Note: Reliability for all measures is provided in Table I. For session-level measures, we report reliability for assessing within-person change (Cranford et al., 2006) noted as R_C (values are comparable to Cronbach's alpha). All measures were administered using Hebrew versions. Example items and endpoints for scales and additional details concerning signal processing, synchrony calculations and statistical analyses are provided in the supplementary material.

Test Anxiety. Test anxiety was measured during the background and the follow-up sessions using the Test Anxiety Inventory (TAI; Spielberger, 2010), in which participants rate how often 20 test anxiety related situations happen to them (e.g., "I freeze in important tests") on a 4 - point Likert-type scale (1—almost never; 4—almost always).

State Test Anxiety. Measured before each session using the state test anxiety scale used by Prinz et al. (2019), adapted from Lawrence and Williams (2013). The scale consists of 6 statements of worries regarding upcoming tests (e.g., "I feel stressed and upset about performing the upcoming test"), rated on a 7—point Likert-type scale (1—completely disagree, 7—completely agree).

Therapeutic Alliance. Measured after each session using the Session Alliance Inventory (Falkenström et al., 2015). The measure consists of 6 statements (e.g., "My therapist and I respected each other"), rated on a 6-point Likert-type scale (0—not at all, 5—completely).

Perceived Session Quality. Measured after each session using the Session Evaluation Scale (SES) 5-item version (Lent et al., 2006). The measure consists of 5 statements (e.g., "I thought that this session was helpful"), rated on a 5-point Likert-type scale (1—strongly disagree, 5—strongly agree), with two reversed items.

General outcome. Measured before and after each session using the Outcome Rating Scale (ORS; Miller et al., 2003), presented as 4 visual slider items, each asking the participant to rate their wellbeing in a different domain (e.g, in close relationships). Scale endpoints are marked as "Very low" and "Very high" wellbeing. Each slider position is mapped to a number between 0 (very low) and 100 (very high).

Overall Satisfaction and Subjective Assessment of fNIRS. Measured on follow-up using two items. Participants rated how satisfied they were with the treatment in general (1—not at all, 4—very satisfied), and how the use of fNIRS affected their experience (1—interfered with my treatment experience very much, 5—improved my treatment experience very much).

Brain Imaging. Brain signals were measured using a BRITE 24 fNIRS measurement system (Artinis Medical Systems). Optode location was chosen using the international EEG 10–20 system (see Figure 3). Measurements were performed at a 50 Hz rate.

Preprocessing was preformed using the HOMER3 Matlab package (Huppert et al., 2009), and involved channel rejection, correction for motion artifacts, conversion from optical density to changes in hemoglobin, and attempts to avoid confounds with physiological processes (Yücel et al., 2021). Channel rejection was performed by discarding channel with above a 0.5 positive correlation between oxyhemoglobin and deoxyhemoglobin (mean rejected channels 12.733(SD 6.022) out of 24). Correction for motion artifacts was performed using Principal Component Analysis (PCA) removing 90% of the variance to correct for motion artifacts. We used a modified Beer–Lambert law to transform optical density values to hemoglobin concentrations. Imaging data were corrected with respect to the participant's scalp thickness, which is calculated based on the participant's age (Scholkmann & Wolf, 2013). We used a 1 Hz low-pass filter to avoid confounds with high-frequency physiological processes (e.g., heartbeat; technically, this was performed before the conversion to hemoglobin concentration).

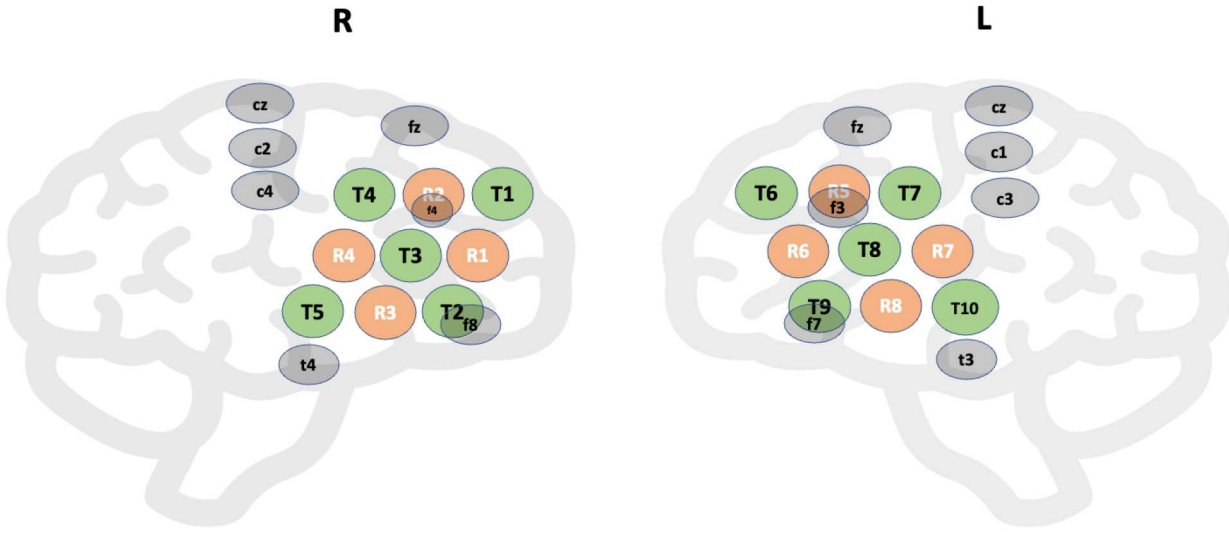

Figure 3. Optode Placement. Note: Optode montage relative to the EEG 10/20 system. The IFG was identified at f7 (left) and f8 (right); Channels T9-R6, T9-R8, T8-R6, T8-R8 were considered the left IFG; Channels T2-R1, T2-R3, T3-R1, T3-R3 were considered the right IFG. Other channels were considered control regions.

We focused on measured changes in brain activity using the oxyhemoglobin signal alone, as it was found to be more sensitive to changes in blood flow in fNIRS research (Hoshi, 2007). In five treatment sessions and three interview sessions one of the imaging recordings failed due to technical issues; In one treatment session and one interview session the recording succeeded but no channel passed data cleaning, leaving 18 session recordings and 12 interview recordings.

Inter-brain Synchrony. Sessions were divided into 1-minute length segments. Optodes were divided to three regions of interest (see Figure 3): left IFG, right IFG, and control regions. Recordings from optodes in each region were averaged. We calculate wavelet transform coherence (Grinsted et al., 2004) using the R biwavelet package (Gouhier et al., 2021) to assess synchrony between each region in the therapist and each region in the participant. After calculating fisher's z values from synchrony r values, outliers of over 5 standard deviations were removed. Out of 865584 synchrony values (one for each specific period, for each specific one minute epoch, for each combination of therapist and patient region), 634 outliers were removed. As no significant differences were found between regions of interest (see also Figure 4) all analyses use mean synchrony across regions.

After averaging synchrony for periods of 1–10 seconds, we dropped the first and last minute of every session to avoid artifacts originating by the very beginning and end of the session. Periods of 1–10 seconds were chosen to avoid artifacts due to physiological processes (with periods below 1 second). Since sessions were of different lengths, we truncated sessions to the length of the shortest session. Thus, when analyzing treatment sessions, we used the first 40 minutes; when analyzing interviews and when comparing treatment sessions with interviews, we used the first 5 minutes. Synchrony was averaged across minutes of the same session (or interview), resulting in a single synchrony value per session.

Statistical Analysis. Unless otherwise stated, data were analyzed using mixed linear models using the R package nlme (Pinheiro et al., 2018) to account for repeated measures. Analyses included random intercepts for each participant, random slopes for all predictor variables, and an autoregression correlation structure to account for similarity between consecutive measurements. Effect sizes were calculated using the methods suggested by Rights and Sterba (2019) using the R package misty (Yanagida, 2022). Partial effect sizes of specific variables were calculated by subtracting the effect size of a model which omitted the examined variable from the total effect size of the model. Analyses of the effects of using fNIRS in a session included a dummy variable which was coded 0.5 for sessions with fNIRS and −0.5 for sessions without. All session-level independent variables were person-mean centered.

Results

Descriptive measures for all variables are provided in Table I.

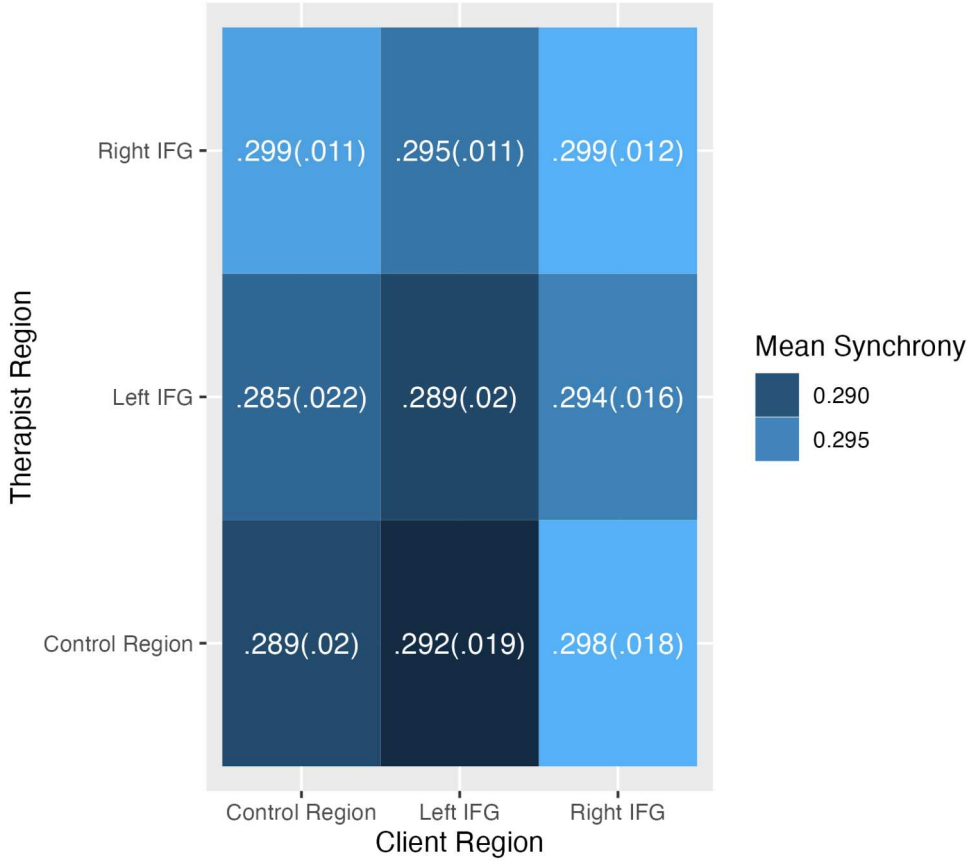

Figure 4. Synchrony Means and Standard Deviations by Brain Region. Note: Values are means(standard deviations) of fisher-z transformed r values for synchrony between each pair of values

The Effect of FNIRS Imaging on Treatment Experience

To rule out the possibility that wearing fNIRS affected the findings, we conducted mixed linear models with fNIRS measurement (a yes/no dummy variable) predicting each outcome variable, controlling for session number as fNIRS was used in earlier sessions (1,3,5 as opposed to 2,4,6). Effect sizes were negligible (all ds < .1) and non-significant, indicating that fNIRS did not have meaningful adverse effects (see Table II).

Regarding treatment satisfaction in general, 5 participants (62.5%) were "very satisfied" and 3 (37.5%) were "pretty satisfied". Regarding the effect of fNIRS measurement on their experience, 1 participant (12.5%) reported it "somewhat improved" her experience, 4 (50%) reported it "did not matter", and 3 (37.5%) reported it "somewhat worsened" their experience.

Table II. Effects of using fNIRS on outcome variables.

		b(SE)	95% CI	t(df)	*p*	d
Alliance Model	Intercept	28.587(2.592)	23.315,33.86	11.03(33.00)	<.001***	
Session Number	0.471(0.269)	−0.076,1.019	1.75(33.00)	.089†		
fNIRS used	−0.165(0.783)	−1.759,1.428	−0.21(33.00)	.834	<0	
Session Satisfaction Model	Intercept	21.35(1.146)	19.018,23.682	18.63(33.00)	<.001***	
Session Number	0.423(0.272)	−0.131,0.976	1.55(33.00)	.130		
fNIRS used	−0.162(0.534)	−1.248,0.924	−0.30(33.00)	.764	<0	
Post Meeting Wellbeing Model	Intercept	236.846(35.792)	164.026,309.666	6.62(33.00)	<.001***	
Session Number	7.742(4.37)	−1.149,16.632	1.77(33.00)	.086†		
fNIRS used	4.844(10.527)	−16.574,26.262	0.46(33.00)	.648	<0	

Note: †$p < .1$ *$p < .05$ **$p < .01$ ***$p < .001$.

Table III. Pre-post treatment differences in outcome variables.

	Mean Difference (SE)	95% CI	t(df)	*p*	d
Baseline and Followup Test Anxiety	−3.12(1.78)	−7.33,1.08	−3.12(7)	.122	0.62
First and Last Meeting State Test Anxiety	−4.88(2.27)	−10.25,0.50	−4.88(7)	.069†	0.76
First and Last Meeting Pre-meeting Wellbeing (ORS)	19.25(25.73)	−41.59,80.09	19.25(7)	.479	0.26
First and Last Meeting Post-meeting Wellbeing (ORS)	50.43(18.02)	6.33,94.53	50.43(6)	.031*	1.06

Note: †$p < .1$ *$p < .05$ **$p < .01$ ***$p < .001$.

Treatment Outcome

We tested person-level changes in test anxiety, as measured in the baseline and follow-up questionnaires, as well as in state test anxiety and overall wellbeing as measured in the first and last meetings, using paired t-test analyses. While all changes were in the expected direction (reduced symptoms, improved wellbeing) with small to medium effect sizes, only changes in post-session ORS were significant, and they did not remain significant after applying Holm's (1979) correction for multiple comparisons (Full results are provided in Table III).

We then assessed change over time in state test anxiety as well as overall wellbeing using multilevel regression analyses using session number to predict each outcome variable. All changes were in the expected direction, and changes in state test anxiety and post-session wellbeing were significant after correction for multiple comparisons (Full results are provided in Table IV).

Inter-Brain Synchrony and Plasticity

To test whether synchrony in the sample was above chance, we created 1000 pseudo-samples by randomly pairing therapist fNIRS recordings of each session with patient recordings from a different session. Mean synchrony in the true sample ($m(SD) = .292(.53)$) was outside of a 95% confidence interval of randomly permuted samples (95% CI .286,.291); only 6 of 1000 permutations had higher mean synchrony than the true sample, as demonstrated in Figure 5.

To examine the association between synchrony and session-level variables including time (session number) and the various outcome measures, we performed mixed regression analyses with each session-level variable predicting synchrony. As we expected, synchrony significantly increased over time (between sessions), with a large effect size ($b(SD) = .007(.002)$, $t(9) = 3.93$, $p = .003$, $d = 1.338$) suggesting that participants' capability to synchronize with the therapist increased over treatment. Analyses of session-level variables showed that synchrony was also significantly associated with state test anxiety, with perceived session quality, and with post-session wellbeing, an association which held even when controlling for pre-session wellbeing. Thus, synchrony was associated with reduced test anxiety symptoms, improved wellbeing, and high perceived session quality. However, contrary to our expectations, synchrony was not positively associated with alliance measures. Findings on synchrony over time are demonstrated in Figure 6. Full results are provided in Table V.

To ensure the robustness of the findings we reanalyzed the data including deoxygenated hemoglobin (in addition to oxygenated) in our measurements, and again using both types of hemoglobin as well as a different motion correction algorithm instead of PCA—correlation-based signal improvement (CBSI; Cui et al., 2010). Synchrony significantly increased over time in all analyses. The associations between synchrony and outcome measures were all significant when adding deoxygenated hemoglobin, but when using CBSI some of them became non-significant. Full results and analysis details are provided in the supplemental

Table IV. Session-to-session change in outcome variables.

		b(SE)	95% CI	t(df)	*p*	d
State Test Anxiety Model	Intercept	30.779(1.551)	27.63,33.927	19.84(35.00)	<.001***	
State Test Anxiety	−1.075(0.494)	−2.077,−0.072	−2.18(35.00)	.036*	.802	
Pre Meeting Wellbeing Model	Intercept	232.962(37.385)	157.067,308.857	6.23(35.00)	<.001***	
Pre Meeting Wellbeing (ORS)	7.244(4.832)	−2.566,17.054	1.50(35.00)	.143	.268	
Post Meeting Wellbeing Model	Intercept	227.335(36.799)	152.55,302.12	6.18(34.00)	<.001***	
Post Meeting Wellbeing (ORS)	10.115(3.691)	2.613,17.617	2.74(34.00)	.010**	.372	

Note: †$p < .1$ *$p < .05$ **$p < .01$ ***$p < .001$.

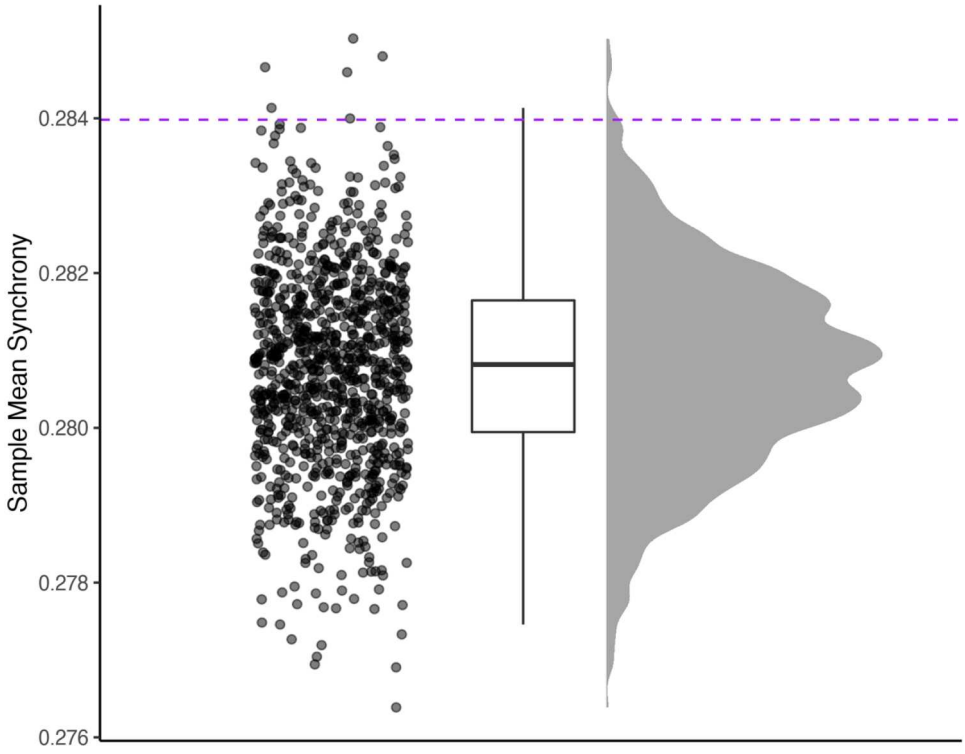

Figure 5. Synchrony in the true sample compared to random permutations. Note: Distribution of synchrony between therapist and patient in 1,000 samples generated by randomly pairing meetings. The dashed line is synchrony in the true sample.

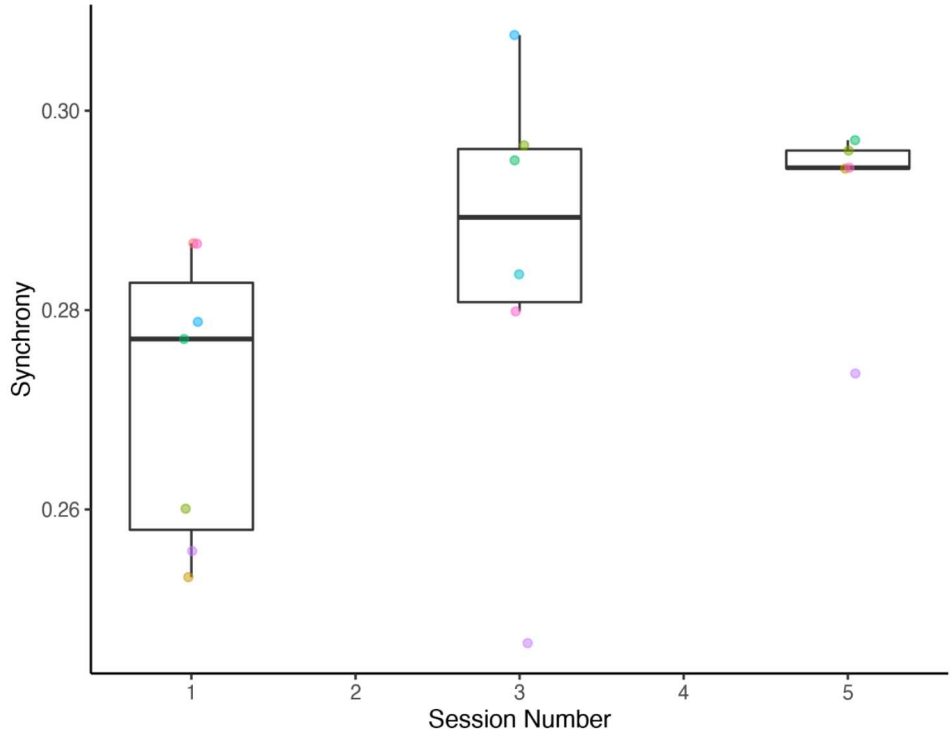

Figure 6. Inter-brain synchrony increases over the course of treatment. Note: Colors indicate different participants; Only session 1,3, and 5 are shown as these were the sessions where synchrony was recorded.

Table V. Associations between session number and outcome variables and synchrony.

		b(SE)	95% CI	t(df)	*p*	d
Session Number Model	Intercept	.29(.005)	.279,.301	59.05(9.00)	<.001***	
Session Number	.007(.002)	.003,.011	3.93(9.00)	.003**	1.437	
State Test Anxiety Model	Intercept	.291(.005)	.28,.303	60.94(7.00)	<.001***	
State Test Anxiety	−.004(.001)	−.005,−.002	−4.84(7.00)	.002**	1.954	
Session Satisfaction Model	Intercept	.294(.006)	.278,.31	45.48(6.00)	<.001***	
Session Satisfaction	.009(.002)	.004,.014	4.14(6.00)	.006**	1.999	
Post-meeting Wellbeing Model	Intercept	.29(.005)	.278,.302	58.53(7.00)	<.001***	
Post-meeting Wellbeing (ORS)	.001(0)	0,.001	5.80(6.00)	.001**	2.202	
Post-meeting Wellbeing Model Controlling for Pre-meeting Wellbeing	Intercept	.291(.005)	.279,.302	58.56(7.00)	<.001***	
Post-meeting Wellbeing (ORS)	.001(0)	0,.001	2.84(5.00)	.036*	< 0	
Pre-meeting Wellbeing (ORS)	0(0)	−.001,0	−0.43(5.00)	.683		

Note: $^{\dagger}p < .1$ $^{*}p < .05$ $^{**}p < .01$ $^{***}p < .001$.

material. To compare synchrony during treatment and during the interviews and between pre and post treatment interviews, we conducted mixed linear analyses with a dummy variable (therapy/interview or pre/post therapy) predicting synchrony. Synchrony was not found to be higher during psychotherapy than during the interviews, showing a small, non-significant *negative* effect instead ($b(SD) = -.007(.01)$, $t(21) = -.758$, $p = .462$, 95% CI −.028,.013, $d = .276$). We also examined whether treatment improved participants' ability to synchronize with the interviewer. Contrary to our expectations, we only found negligible change between pre-treatment and post-treatment interviews ($b(SD) = -.001(.007)$, $t(4) = .088$, $p = .934$, 95% CI −.019,.018, $d = .034$).

Discussion

The current study was the first to use fNIRS hyperscanning over the course of a full (albeit short) course of psychotherapy. Our findings suggest that the use of fNIRS was well-received by participants and did not interfere with positive treatment outcomes. In line with our hypothesis, the findings provide initial evidence of inter-brain plasticity in the IFG during psychotherapy, i.e., an increase in inter-brain synchrony over treatment. Critically, this increase was associated with symptom reduction and improved wellbeing. However, it did not generalize to a new person, and synchrony was not associated with a stronger therapeutic alliance.

Treatment Outcome

The current study was not designed or powered to demonstrate treatment efficacy. Indeed, pre-post comparisons of outcome measures did not yield significant results. However, there are several indications that the treatment was effective. First, effects were in the expected direction, with meaningful effect sizes. Second, session-level analyses, which have higher statistical power due to repeated measures, did reveal a significant reduction in symptoms and improvement in wellbeing. Finally, reduction in symptoms was larger than during the comparable period of a larger trial of this treatment (Test anxiety mean change −3.125 in the current study, compared to 2.2 between first baseline to first followup in Prinz et al., 2019). Of course, as there was no control condition, these results cannot be conclusively attributed to treatment effects based on the current study alone, although the aforementioned existing trial did support causal effects for the treatment protocol (using a multiple baseline design).

Reception of FNIRS During Treatment

Differences between sessions with and without fNIRS were negligible with respect to therapeutic alliance, wellbeing, or perceived session quality. While some participants reported being mildly inconvenienced by the method, satisfaction with the treatment as a whole was high. Additionally, there was no attrition. These findings suggest that fNIRS measurement does not meaningfully interfere with treatment, supporting the use of fNIRS as a measure in neuroscientific psychotherapy research. Anecdotally, we believe that the use of fNIRS only in alternating sessions contributed to the tolerance of this method by participants and would be wary of using it in all sessions. Clinically, it allowed the therapist to assess whether patients were behaving differently during imaging and to watch for potential adverse effects.

Synchrony, Psychotherapy and the Therapeutic Alliance

Inter-brain synchrony was associated with less test anxiety symptoms, higher session satisfaction and improved wellbeing. This suggests that inter-brain synchrony tracks the effectiveness of interpersonal interaction between therapists and patients during therapy, ultimately leading to better outcomes. However, our design is not sufficient to conclude whether changes in synchrony are *driving* the changes in outcomes or are a byproduct of these changes.

We did not replicate Zhang and colleagues' (2018) findings of increased brain synchrony in therapy compared to casual conversation, and an association between therapeutic alliance and brain synchrony. Regarding the synchrony-alliance association, three of the eight participants consistently reported near-maxima alliance scores (35 or 36 out of 36), suggesting that a ceiling effect might have influenced results. Omitting these participants results in a positive, albeit non-significant, association in the expected direction with $d = 0.6$. Of course, this is an exploratory analysis based on an even lower sample size than the original one which should not be used as an indication of an effect, but it does indicate that ceiling effects are dominating the results of the full analysis. To avoid ceiling effects, researchers could use longer instruments to measure the alliance (e.g., the Working Alliance Inventory; Horvath & Greenberg, 1989), or recruit populations with more severe disorders which would be less likely to report such high alliance scores; alternatively, with larger sample sizes (which would be advisable in any case) having some participants with ceiling effects would be less of an issue.

An alternative explanation for the null finding regarding the comparison between synchronization in therapy as opposed to casual conversation could be the different model of casual conversations. Zhang and colleagues (2018) used unstructured small talk as a model for casual conversation, as opposed to the current study which used clinical interviews. As the interviewers were psychology students and the content of the conversations was clinical, the interviews might have tapped into the same therapeutic processes which elevated synchrony above small talk in the 2018 study. Additionally, the interviews were more structured than either small talk or therapy; the specific questions and components of the interview might have served as a consistent stimulus that increased synchrony (Golland et al., 2015).

Finally, both null findings (with regard to the synchrony—alliance association as well as the difference between therapy and casual conversation) might be due to the role of different brain regions. Zhang and colleagues (2018) focused on the temporoparietal junction [TPJ] as opposed to the IFG, which is the focus of the current study. The TPJ is considered to be part of the theory of mind system (Carrington & Bailey, 2009; Schurz et al., 2014), which is related to the ability to identify others' mental states, while the IFG is part of the observation-execution system (Shamay-Tsoory et al., 2019), which is involved in observing actions and executing similar actions. It could be the case that synchrony in the TPJ reflects instances in which the therapist identifies patients' mental states but does not engage in synchronized action based on these observations, and that such instances are more common in therapy than in small talk and contribute to the therapeutic alliance.

Importantly, while these explanations should be considered when planning future studies, it should be noted that any null results may simply be the result of the small sample size, and as such should be interpreted with caution.

Inter-brain Plasticity

Our findings have demonstrated a gradual increase in inter-brain synchrony over the course of therapy. This is the first study to support the notion that inter-brain plasticity—i.e., changes in therapist's and participant's brains which afford higher synchrony—has occurred. It is possible that with repeated empathic reactions, intra-brain synchrony strengthens, resulting in increased behavioral synchrony. Learning studies indicate that after training, consolidation-related "off-line" processes lead to lasting neuronal changes (Caroni et al., 2012). Thus, when the client and therapist meet in repeated sessions, both may display an improved ability to attune and align with each other. A potential physiological mechanism underlying long-term changes in synchrony between brain regions may be associated with a reactivation process occurring during consolidation. The "reactivation hypothesis" suggests that regional activity recorded during training re-emerges during consolidation (Rasch & Born, 2007). Reactivation of synchrony during consolidation may trigger greater synchrony between brain regions. The change in synchrony between regions in two interacting brains during psychotherapy may be reactivated during consolidation. This could result in brain regions in different individuals adapting their activity to become more coupled with other regions after training in psychotherapy. While learning could involve generalization such that the client will become more capable of becoming aligned with

others even when the therapist is not present, in the current study inter-brain synchrony did not generalize to an encounter with an interviewer at the end of treatment. Still, it could be the case that a longer treatment is required to achieve a generalized increase in synchrony, or that the interview task was too structured to show changes in participants' capability to synchronize. As the current study used a correlational design, it cannot conclusively rule out the possibility that inter-brain synchrony gradually increased due to some other mechanism. However, the fact that the change in synchrony was limited to the relationship with the therapist and did not generalize to the interviewers suggest that whichever process lead to the change was specific to the therapy.

As for the therapeutic implications of inter-brain plasticity, higher synchrony was also associated with symptom reduction and with an increase in wellbeing over the course of each specific session. Thus, it is possible that some therapeutic mechanisms of change manifest on a neural level as inter-brain plasticity. Current theory regarding synchrony in psychotherapy (Koole et al., 2020) posits that consistently high synchrony (on the neural or behavioral levels) is associated with a consistently strong alliance, which leads to positive change in higher-level processes such as emotion regulation. If the findings of the current study are corroborated in larger samples, it would suggest that therapy is not only associated with consistently high synchrony (Wiltshire et al., 2020), but also with a gradual increase in the capacity to synchronize. This increase—whether a causal factor in and of itself, or a marker of other processes—points to a possible additional mechanism of change in which the very interpersonal experience in therapy is not only consistently positive, but also gradually improving in quality.

Beyond these theoretical implications, an association between inter-brain plasticity and therapeutic change would allow for the use of in-session imaging as a continuous measure of therapeutic change throughout the session. Future studies could examine how specific in-session techniques affect inter-brain synchrony. It would also point to the possible effectiveness of neural-based interventions, which could be as simple as therapists and patients performing a synchronized tapping exercise to increase inter-brain synchrony (Kurihara et al., 2022). However, the current design cannot rule out that inter-brain plasticity could simply be a side effect of successful therapy. Even in that case, given the non-clinical research linking inter-brain synchrony to better interpersonal interaction (e.g., Czeszumski et al., 2022), inter-brain plasticity could be an additional benefit of successful therapy.

Limitations

The main limitation of the current study is its small sample size, exacerbated by missing data for some sessions, and single therapist. This could have led to spurious correlations being found between study variables. As such, results should be seen as pending replication. Specifically, future studies should include larger sample sizes.

The lack of power might also explain why no differences were found between IFG and control regions, limiting the ability to implicate the IFG specifically. Additionally, the therapist and interviewers were not blinded to study hypothesis, although this is mitigated by the fact that brain synchrony is not a self-report measure and is not even wholly dependent on a single person and as such, cannot be easily manipulated. Another limitation of note is that differences in inter-brain synchrony can be the results of other processes than the progression of therapy (e.g., changes in levels of tiredness). However, if the changes are the result of another process, that process would have to progress systematically alongside treatment sessions—for example, there is no reason why patients should be systematically more tired during the fifth session than the first session, which are conducted weeks apart. Finally, the study design does not allow us to causally interpret the association between synchrony and symptom change. Future studies could overcome these limitations by using a multiple baseline design, as well as longer treatment protocols, to attempt to understand the causal direction of these effects, by including blinded interviewers and therapists, and by examining additional brain regions.

Conclusion

The current study demonstrated that fNIRS measurement during psychotherapy is a viable research method that at least in a small sample did not interfere with therapy; we encourage future research to use fNIRS to examine inter-brain plasticity and other single- and dual-brain processes in psychotherapy. Here we provided preliminary evidence that inter-brain synchrony increases during psychotherapy, which may indicate the occurrence of inter-brain plasticity, and that synchrony was associated with lower symptom and higher wellbeing. While the current studies' findings require replication due to the small sample size, they suggest that

this process of improved synchrony should be explored further as a possible mechanism of change.

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No potential conflict of interest was reported by the author(s).

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Supplemental Data

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