

Simulation and social behavior: an fMRI study of neural processing during simulation in individuals with and without risk for psychosis

Sarah Hope Lincoln,¹ Laura T. Germine,^{2,3} Patrick Mair,¹ and Christine I. Hooker⁴

¹Department of Psychology, Harvard University, Cambridge, MA 02138, USA, ²Department of Psychiatry, Harvard Medical School, Boston, MA 02115, USA, ³McLean Hospital, Belmont, MA 02478, USA, and

⁴Department of Psychiatry and Behavioral Sciences, Rush University Medical Center, Chicago, IL 60612, USA

Correspondence should be addressed to Sarah Hope Lincoln, 33 Kirkland Street, Cambridge, MA 02138, USA. E-mail: sarahhope.lincoln@gmail.com

Abstract

Social dysfunction is a risk indicator for schizophrenia spectrum disorders, with at-risk individuals demonstrating a range of social behavior impairments. Variability in social ability may be explained by individual differences in the psychological processes of social behavior. In particular, mental simulation, the process by which an individual generates an internal representation of the thoughts or feelings of another, may explain variation in social behavior. This study investigates the neural process of simulation in healthy individuals and individuals at risk for psychosis. Using a novel fMRI pain paradigm, individuals watch videos of another person's hand or foot experiencing pain. After each video, individuals are asked to simulate the observed painful situation on their own hand or foot. Neural activity during simulation in the somatosensory cortex was associated with real-world self-reported social behavior, such that a stronger neural response in the somatosensory cortex was associated with greater rates of positive social experiences and affective empathy across all participants. These findings suggest that the neural mechanisms that underlie simulation are important for social behavior, and may explain individual variability in social functioning in healthy and at-risk populations.

Key words: simulation; mentalizing; social behavior; psychosis

Introduction

Our capacity to understand the mental states of others is fundamental to human relationships. Several theories regarding how we understand the minds of others have been proposed. For example, 'mental simulation' is the process of understanding another person's mental state by generating an internal representation of the other's experience (Gallese, 2007). In another theory, 'theory-theory', individuals understand the

mental states of others by drawing upon established concepts of mental states and principles of how they function (Mahy et al., 2014). Recently, the field has moved away from these theories as competing, and instead, has focused on the integration of these theories (Keysers and Gazzola, 2007; Redcay and Schilbach, 2019). Understanding the neurobiology supporting these theories is critical in identifying the mechanisms that support social cognitive processes, which in turn support social behavior, and

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ultimately, social functioning (Kennedy and Adolphs, 2012). Working from this model, disruption in the neural mechanisms may contribute to social dysfunction and variability in social behavior across individuals.

In order to assess a range of social abilities, this study focuses on social behavior differences within and across individuals at clinical high risk (CHR) for psychosis and healthy controls (HC). Social dysfunction is a primary risk factor for psychotic disorders (Tarbox et al., 2013), significantly contributes to overall disease burden, and does not abate alongside positive symptoms (Holley, 2010). Research consistently demonstrates that individuals at a CHR for psychosis—individuals with attenuated positive symptoms—have greater social impairment than demographically matched individuals without psychosis risk (Ballon et al., 2007; Addington et al., 2008; Jang et al., 2011). The mechanisms that support healthy social functioning, which, therefore, may also explain social deficits, remain an important area of study in psychotic disorders. Moreover, by investigating differences in social behavior across at-risk and healthy populations, we are able to test a wider range of variability in individual differences across social behavior than observed with only healthy participants. Given that we expect the same neural mechanisms to underlie individual differences in social behavior in at-risk and healthy participants, this increased variability strengthens our methodology.

The goal in this current study is to focus on the specific mechanism of simulation, i.e. the generation of an internal representation of another's experience within ourselves. The theory of mental simulation maintains that when we imagine the action, perception or emotion of another person, we elicit neural responses in the same regions associated with the performance or experience of that action, perception or emotion. Though not the only method by which we can understand the mental states of others (Apperly, 2009), simulation offers one neurobehavioral mechanism by which mental inference occurs.

Through the process of simulation, the observer understands the experience of another by internally representing the emotions, beliefs or intentions of the other (Mitchell et al., 2005). Using personal experiences as a reference, the observer makes inferences about others' mental states. Simulation occurs on an implicit or automatic level, such as processes like motor-mimicry and imitation, referred to as 'mirroring.' However, simulation is also an explicit, strategic process recruited for mental state reasoning, referred to as 'mentalizing.' Mirroring involves the perception and subsequent vicarious experience of another person's mental state and is often linked with imitation (Waytz and Mitchell, 2011), whereas mentalizing works in the absence of an external cue, such that the individual imagines how he or she would feel in a given situation, and then projects that interpretation on to another.

The primary brain regions implicated in simulation, particularly through mirroring or imitation, are the parieto-frontal network (including the motor and somatosensory cortices), anterior cingulate cortex and insula (Rizzolatti and Fabbri-Destro, 2008). For example, the somatosensory cortex is recruited both in the observation of others' emotional facial expressions (Adolphs et al., 2000, 2003; Pourtois et al., 2004), bodily sensations and physical experiences (e.g. touch) (Keysers et al., 2004; Blakemore et al., 2005). Additionally, studies show that these same somatosensory regions are necessary for social cognitive tasks such as empathy and theory of mind (Adolphs et al., 2003; Avenanti et al., 2005). Importantly, Hooker and colleagues (Hooker et al., 2008) found that greater activity in somatosensory related cortex, when inferring the emotion of another person,

was related to greater self-reported empathy in daily life. These findings are consistent with the theory that, in the absence external cues, people generate an internal, neural representation of an emotion in order to understand the experience of another person.

Though the interpretation of this body of work is that individuals generate a neural representation of the target experience (i.e. thought, emotion or action), this interpretation has not been directly tested. Previous studies focused on mirroring, rather than mentalizing, often employ tasks combining the actions of observe, imitate and execute (Montgomery and Haxby, 2008; Becchio et al., 2012; Thakkar et al., 2014). Thus, much of the evidence for the neural basis of simulation is indirect. Prior studies have assumed the internal representation of a stimulus, but study designs fail to empirically test this assumption.

Furthermore, prior research on the neural mechanisms underlying simulation fails to link neural activity with behavioral measures. While studies make claims that these neural processes may facilitate emotion understanding in others, (Olsson and Ochsner, 2008; Shamay-Tsoory, 2011) and explain social cognitive and social functioning impairments in disorders such as autism (Spunt and Lieberman, 2012), these claims have not been empirically tested. A primary goal of this study is to investigate whether neurobiological deficits in simulation contribute to or are causally related to social dysfunction in individuals at risk for psychosis.

Current study design

The present study identifies neural mechanisms involved in the explicit and effortful use of simulation and tests whether individual differences in these neural mechanisms predict individual engagement in social behaviors. To directly test the neural mechanisms of simulation, we used an functional magnetic resonance imaging (fMRI) task that includes both 'observation' and 'simulation' of the stimulus, using a pain paradigm (Figure 1). In this novel task, participants watch videos of another individual experiencing pain in/on the hand or foot. This pain-observation condition is similar to previous tasks that look at brain activity in response to an individual's observation of another individual in pain (Jackson et al., 2005, 2006). After observation, once the stimulus is removed, participants are asked to 'imagine' how unpleasant the previously observed experience would be for them. Unique to this task, this second condition directly elicits simulation. Activity in the somatosensory cortex in the absence of a stimulus would support evidence of a simulation process. By capitalizing on our knowledge of the homunculous (Nakamura et al., 1998), we localized the hand and foot areas for each individual in our study. While in the scanner, participants rubbed their hands or feet together, which allowed us to functionally localize the individualized hand and foot regions of the somatosensory cortex. We used these functionally identified regions to test whether the simulation task recruits these regions. The strength of activity in the somatosensory cortex, in particular the hand and foot areas, shows the degree to which these neural regions are recruited, more directly testing the simulation process.

To date, the literature on simulation processes in psychotic disorders is mixed. Some studies have found neural deficits in simulation-related processes in individuals with schizophrenia vs HC (Thakkar et al., 2014), while other studies show no difference between individuals with schizophrenia and controls (McCormick et al., 2012; Horan et al., 2014; Mukerji et al., 2018). We aim to clarify and extend this work in at-risk populations using a

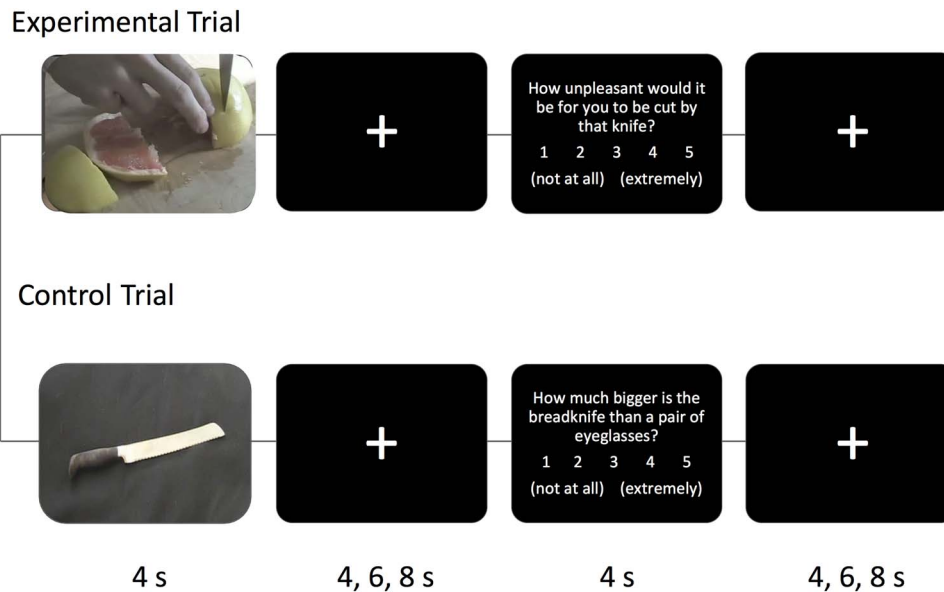


Fig. 1. Simulation task. In the experimental trial participants view hand/foot pain (e.g. hand cut by knife), followed by a jittered fixation cross, and then a screen prompting the participant to determine how unpleasant the previously viewed experience would be for them on a 1–5 point scale, followed by a jittered fixation cross. In the control trial, participants view an object, followed by a jittered fixation cross and then a screen prompting them to determine the relative size of the object on a 1–5 scale, followed by a jittered fixation cross.

novel fMRI task. We hypothesized that CHR participants, relative to HC, would show less simulation-related activity as demonstrated by decreased activity in the hand/foot regions of the somatosensory cortex during the simulation > observation conditions. Additionally, we hypothesized that the degree of activity in these regions would be positively related to three aspects of daily social behavior: affective empathy (AE), perspective taking (PT) and positive social experiences (PSE). We hypothesize that simulation, as the mechanism supporting social thoughts and behavior, may directly support AE, the understanding of others' emotional experiences, and PT.

Methods

Participants

Twenty-one CHR participants (7F/14M) and 19 HC participants (9F/10M) completed this study. Individuals were recruited from the greater Boston community. Inclusion criteria for all participants were (i) age between 15 and 35 years, (ii) ability to give informed consent or assent (participants <18 years) and (iii) English as a first language. CHR individuals were identified as those who met a symptom intensity level of 3–5 on at least one of the five positive symptom categories (i.e. unusual thought content, suspiciousness/persecutory ideas, perceptual aberrations, grandiosity and disorganized speech) assessed by the Structured Interview for Prodromal Syndromes (SIPS). Of note, CHR participants were not required to meet the temporal or frequency criteria of positive symptoms that are typically required for a prodromal diagnosis.

Exclusion criteria for all participants included IQ < 70, current or past psychotic disorder, lifetime substance dependence, substance abuse within the last 3 months, head injury, history of neurological problems or MRI contraindications. Additionally, HCs were excluded for any current or past psychiatric disorder.

Clinical assessments

All participants completed three clinical interviews: (i) the structured clinical interview for the DSM-IV (SCID) (First et al., 2002) to assess for current axis I disorders; (ii) the SIPS (Miller et al., 2003) to assess for the presence of prodromal symptoms and (iii) the global functioning scale: social and role (Kay et al., 1987; Cornblatt et al., 2007) to assess symptom severity. Additionally, all participants completed the vocabulary and matrix reasoning subscales of the Wechsler abbreviated scale of intelligence (Wechsler, 1999).

fMRI tasks

Simulation task. In order to test whether simulation-related activity differed between at-risk and healthy individuals, we created an fMRI task of pain observation and simulation conditions across three trial types: hand, foot and control. Using an event-related design, trials are presented in a fixed randomized sequence. In the experimental trials (hand/foot), participants view a fixation cross, then observe a short (4-s) video of another person's hand or foot encountering a painful situation (e.g. hand slammed in a car door, hammer dropped on foot, etc.), after which a fixation cross appears. Next participants are prompted to evaluate how unpleasant the previously viewed experience would be for them. Specifically, they saw the question 'How unpleasant would it be for you to be [cut by that knife]?' This question is the 'simulation' condition; there is no visual content of a hand, foot or object; thus, the individual must imagine the experience. Using a five-button box, the participant rated the level of unpleasantness from 'not at all unpleasant' (1) to 'extremely unpleasant' (5).

During control conditions, participants observe a static object and are asked to imagine that object's size relative to a different object. The control trial begins with a fixation cross, followed by a 4-s still video shot of an object used during the hand/foot trials (e.g. a kitchen knife), followed by a fixation cross. Next

participants are prompted to compare the object's size relative to a newly introduced object, not pictured, along a five-point rating scale. Participants saw on the screen 'How big is the [knife] compared to a [penny]?' Using the five-button box, participants rated the comparison from much smaller (1) to much bigger (5). The inclusion of this condition controlled for general visual representation of an item previously viewed *vs* specific representation of an emotional experience in the pain conditions. Across three 12-min runs, there were a total of 32 videos in each type of trial (hand, foot and control). Fixation crosses were jittered at 4, 6 and 8 s. All stimuli were presented using Matlab software.

Localizer task

In addition, a 'localizer' scan was conducted to functionally identify or 'localize' each participant's hand and foot region of the somatosensory cortex. During the localizer scan, participants' movement of their hands and feet allowed for exact identification of hand and foot regions of the somatosensory cortex. Thus, we use these functionally defined regions of interest (ROI) to identify neural activity during the simulation task. The localizer run included five, 20-s blocks of movement and stimulation for both the hands and feet, with 12-s rest periods in between each movement block. Participants were instructed to rub their hands or feet together at different times. This task allowed us to identify each individual's hand and foot region of the somatosensory and motor cortices. The strength of activity in these somatosensory cortex regions was used to indicate the degree to which this region is recruited for simulation. In other words, neural activity in these localized regions during simulation indicates the generation of a neural representation of the hand/foot, and this design allowed us to directly test the simulation process.

fMRI image acquisitions

Images were acquired on a 3.0 Tesla Siemens Tim Trio scanner using a 32-channel head coil. Echoplanar (EPI) image acquisition parameters: 40 oblique-axial slices with $3 \times 3 \times 3$ mm isotropic voxels; TR = 2560; TE = 30, flip angle = 85° , FOV = 216×216 mm. Anatomical T1-weighted resolution scan (MEMPRAGE) acquisition parameters: 176 axial slices, $1 \times 1 \times 1$, TE (multi-echo): 7.22 ms; TR: 2530 ms; flip angle = 7° ; FOV = 256×256 mm.

fMRI analysis

Data analysis used SPM8 (Wellcome Department of 307 Cognitive Neurology, London, United Kingdom; <http://www.fil.ion.ucl.ac.uk/spm/software/spm8>) within the general linear model (GLM) framework. Preprocessing included slice timing, realignment to the mean image across all runs, coregistration to the structural image, normalization to the MNI template and smoothing with an 8-mm Gaussian kernel. All analyses included a high-pass filter (128 s).

Task-related activity for simulation and localizer tasks was modeled separately. For the simulation task, we modeled hemodynamic dynamic responses for each of the six conditions of interest: observation hand; observation foot; observation control; simulation hand; simulation foot and question control. We created contrasts for each condition *vs* baseline (black fixation cross on white background). Primary contrasts were observation and simulation *vs* control conditions (e.g. observation hand > observation control); simulation hand > question control). The artifact detection toolbox (Gabrieli-Whitfield;

http://www.nitrc.org/projects/artifact_detect/) was used to identify outlier scans in global signal intensity ($\pm 3SD$) and movement (>3 mm). These volumes were included in the GLM as nuisance regressors. In the localizer task, we modeled hemodynamic response at the onset of each condition block (i.e. hand rubbing and feet rubbing) for a 20 s duration. Contrasts were created for hand motion > fixation and foot motion > fixation.

Regions of interest definition and analyses

We created ROIs for the somatosensory cortex hand/foot areas for each participant based on the functional localizer. Using the MarsBar toolbox within SPM8, left and right hemisphere hand/foot ROIs were defined by 10 mm spheres centered at the positive maxima in the hand motion > fixation contrast and the foot motion > fixation contrast, respectively. For each participant, simulation hand > control question contrast estimates were extracted from the left and right hemisphere hand ROIs, and simulation foot > control question contrast estimates were extracted from the left and right hemisphere foot ROIs. These values provide the strength of the neural representation of the imagined sensorimotor pain experience in each participant's hand/foot region of the somatosensory cortex.

Diary

After the behavioral session and fMRI scan, participants completed a 7-day online daily diary, approximately 15–30 min per evening. The diary focused on participants' social interactions, and their thoughts, feelings and experience of these interactions. Participants received compensation for each completed diary and additional 'bonus' compensation for completing seven consecutive diary entries. The full diary included additional questions relevant to other studies, but not this study, and therefore, are not investigated or reported here. We focused on the three social constructs that were central to our hypotheses: positive social experience (PSE: 3-items), affective empathy (AE: 2-items) and perspective taking (PT: 3-items). Specific items and associated data are listed in the Table 1. On average participants completed 5.85 of 7 days, with CHR participants ($M = 5.28$) completing fewer days on average than controls ($M = 6.53$; $P = 0.02$).

Data analytic overview

First, to verify expected activation in the localizer-defined ROIs, we conducted paired *t*-tests to test whether neural activity during the simulation condition was greater than the control condition (e.g. simulation hand/foot > control question). We examined differences in these conditions for the right hand, left hand, right foot and left foot. Second, to test group differences in simulation activity between CHR and HC, we conducted a multivariate analysis of variance comparing these groups for each contrast (e.g. simulation right hand > control question). We chose to examine differences between contrasts, rather than individual conditions as done in the first step, in order to reduce the overall number of tests conducted.

Finally, given the focus on individual differences within the relationship of simulation related brain activity and social functioning, we used structural equation modeling (SEM) to model the relationship between fMRI measures of simulation and daily diary reports of social behavior. SEM was used to represent item responses in the daily diary as manifest expressions of underlying latent variables (e.g. PSE). Additionally, as measures of these

Table 1. Demographics

	CHR for psychosis N = 21	Healthy participants N = 19	Differences between groups
Gender (F/M)	14M/7F	10M/9F	$\chi^2 = 0.82, P = 0.36$
Age	22.05 (4.48)	22.58 (3.34)	$t(38) = 0.42, P = 0.68$
Education	14.10 (2.40)	15.21 (1.32)	$t(29.75) = 1.80, P = 0.08$
IQ	108.10 (17.29)	117.00 (10.37)	$t(33.23) = 2.00, P = 0.054$
SIPS scale			
Positive symptoms	12.38 (4.79)	0.44 (.98)	$t(21.95) = 11.15, P < 0.001$
Negative symptoms	6.57 (5.25)	0.61 (1.24)	$t(22.40) = 5.05, P < 0.001$
Disorganized symptoms	2.76 (1.70)	0.39 (0.61)	$t(25.73) = 5.97, P < 0.001$
General psychopathology symptoms	4.43 (3.96)	0.17 (0.51)	$t(20.79) = 4.89, P < 0.001$
Global functioning scale			
Social	7.38 (1.63)	9.11 (0.99)	$t(33.56) = 4.09, P < 0.001$
Role	6.81 (1.44)	8.95 (0.71)	$t(29.73) = 6.06, P < 0.001$
Behavioral ratings scan task (range 1–5) ^a			
Hand pain/unpleasantness trials	2.82 (0.75)	2.66 (0.87)	$t(34) = 0.59, P = 0.56$
Foot pain/unpleasantness trials	2.83 (0.75)	2.72 (0.86)	$t(34) = 0.43, P = 0.67$
Average pain/unpleasantness rating (hand/foot)	2.83 (0.74)	2.69 (0.86)	$t(34) = 0.52, P = 0.61$
Control trials (size estimate of objects)	2.64 (1.19)	2.34 (0.61)	$t(34) = 0.96, P = 0.34$

^aPain Question: 'How unpleasant would it be for you to be cut by that knife?'; Size Question: 'How much bigger is the breadknife than a pair of eyeglasses?'

constructs are typically correlated, an SEM model can account for both latent variables and potential covariance. Neural activity for simulation (i.e. fMRI contrast: simulation hand/foot > control question) in each ROI served as the exogenous variables, and the three latent constructs (PSE, AE and PT) the endogenous variables. SEM with maximum likelihood (ML) estimation was conducted using analysis of moment structures (AMOS). Model fit was assessed with: (i) comparative fit index, (ii) the root-mean-squared error of approximation (RMSEA). We estimated item loadings in the measurement part of the model (diary variables), and path coefficients (regression parameters) for the structural part of the model. In order to apply ML-based procedures, the indicators should be a multivariate normal distribution. Since our data deviated slightly from normality, with a small sample size (30 participants), we used robust standard errors. A measurement model was estimated to create latent variables for PSE, AE and PT, where the mean scores from each of the items comprised the indicator variables.

Results

Behavioral results

Table 1 shows demographic information. No significant differences emerged between groups for age, gender or IQ ($P_s > 0.054$). As expected, the CHR group had significantly greater positive, negative, disorganized and general SIPS symptoms than the HC group. Additionally, the CHR group showed significantly greater impairment in social functioning on the global functioning scale: social ($P < 0.001$), compared to controls. For the diary social constructs, PSE, AE and PT, we note that CHR participants had slightly lower ratings than HCs ($P_s < 0.021$). However, after Bonferroni-correction for multiple comparisons, no significant group differences remained.

Simulation results

First, we examined whether participants had significant simulation-related activity in the individually localized hand and foot regions. If participants used simulation, we expected neural activity in the somatosensory/somatomotor cortex of

each individual's hand/foot region. For these analyses, we see significantly greater activation in the simulation relative to control conditions for the right hand ($t = 3.54, P = 0.001$), right foot ($t = 3.55, P = 0.001$) and left foot ($t = 2.82, P = 0.007$). These findings are consistent with our hypothesis, and indicate that when imagining a painful experience during the simulation condition, the specific regions (i.e. right hand, right foot and left foot) of the somatosensory cortex were recruited more than when imagining an object in the control condition. Contrary to our hypothesis, we do not observe greater simulation activity in the left hand. Rather, *post-hoc* analyses reveal greater activation to the control relative to simulation condition for the left hand ($t = -3.63, P = 0.001$). Figure 2 depicts the strength of neural activity in the right and left hand and right and left foot across the simulation and control conditions.

Group differences in simulation activity

To test for group differences in simulation-related activity between HC and CHR, we conducted a multivariate ANOVA on neural activity for the simulation hand/foot condition relative to the control question condition (i.e. the fMRI contrast: simulation hand/foot > control question) in the right hand, right foot and left foot. No significant differences emerge between CHR and HC for simulation related activity ($F = 0.87, P = 0.465, \eta^2 = 0.07$).

Relationship between simulation-related activity and social functioning

SEM was used to examine the relationship between simulation-related neural activity, based on the contrast simulation hand/foot > control question, and social behavior as assessed in the diary. Neural activity in the left and right foot ROIs was highly correlated ($r = 0.75$); thus, these regions were averaged and included in the model as one variable representing activity in the left and right foot (LRF) ROIs. Since there was no simulation-related activity in the left hand ROI, this variable was dropped from the model. The SEM analysis examined the fit of the model, with simulation activity in the right hand (RH) and combined left and right foot (LRF) as predictors of diary constructs AE, PT and PSE. Means and standard deviations for individual items

Table 2. Daily diary variables and individual items

	All subjects M (s.d.) N = 40	CHR M (s.d.) N = 21	HC M (s.d.) N = 19
AE			
I felt empathy or sympathy for someone else because of their difficult circumstances (AE 1)	2.39 (0.81)	2.14 (1.15)	2.63 (1.22)
I had warm, affectionate feelings for someone else (AE 2)	3.07 (1.00)	3.12 (1.22)	2.99 (1.43)
PT			
I made an effort to understand another person's experience or point of view (PT 1)	2.38 (0.82)	2.15 (1.18)	2.53 (1.18)
I tried to imagine what another person might be thinking or feeling (PT 2)	1.84 (0.52)	1.89 (0.93)	1.77 (0.90)
I tried to see things from multiple different points of view (PT 3)	2.26 (0.85)	2.02 (1.11)	2.54 (1.25)
PSE			
I socialized with other people, and I enjoyed it (PSE 1)	3.61 (0.72)	3.36 (1.06)	3.95 (0.84)
I socialized with other people, and I look forward to socializing again in the near future (PSE 2)	3.62 (0.77)	3.42 (1.05)	3.97 (0.79)
I socialized with other people, and I felt like other people liked me (PSE 3)	3.52 (0.78)	3.38 (1.00)	3.84 (0.77)

Notes: Participants rated each statement on a scale from 1 to 5 every evening for 7 days. Data below are average rating over 7 days.

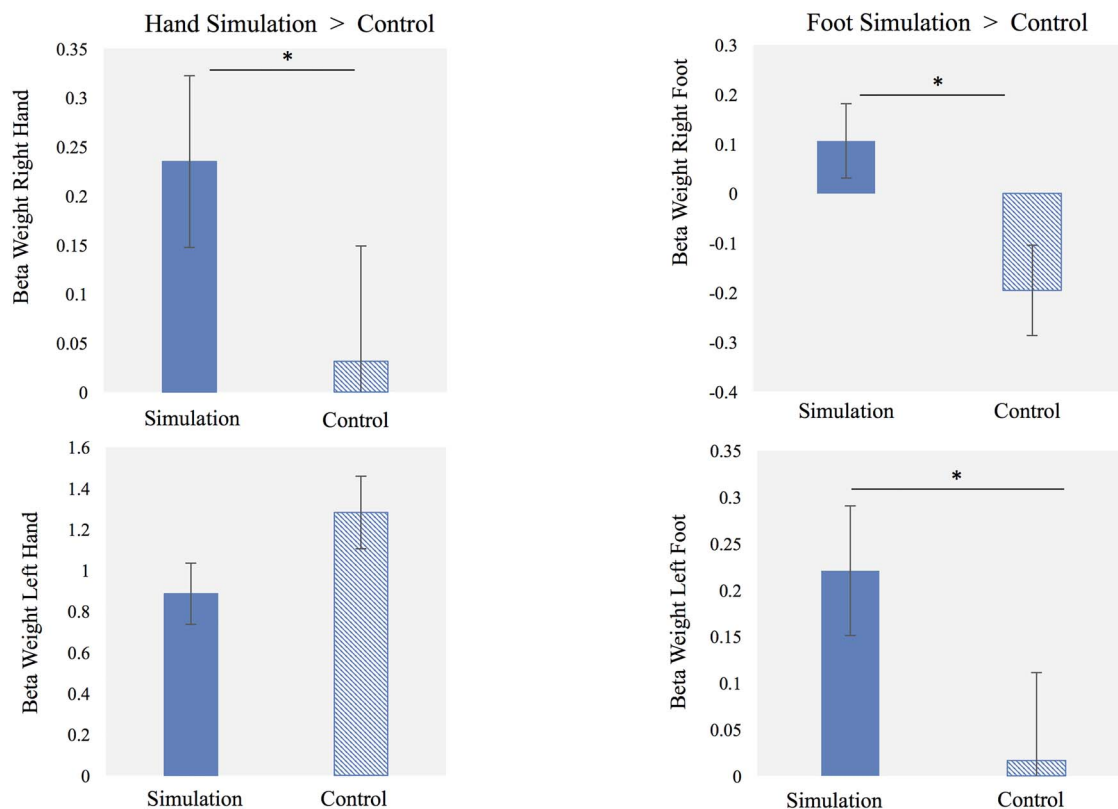


Fig. 2. Neural contrast plots for neural activity all participants ($N = 40$) during the evaluation (i.e. simulation) of hand or foot pain relative to evolution of object size (contrasts: hand simulation > control and foot simulation > control) in the individually localized ROIs for right and left hand, and right and left foot. Post-hoc contrasts reveal a significant difference for simulation > control in ROIs for the right hand ($P = 0.001$), right foot ($P = 0.001$) and left foot ($P = 0.001$). No significant emerged in the left hand ROI.

making up the latent variables are included in Table 2. We hypothesized that simulation-related activity in the RH and LRF would partially explain social behavior, such that greater activity would be associated with better social processes. The SEM fitted to assess the hypothesized model is depicted in Figure 3. This model fit the data well with an RMSEA=0.07, CFI=0.99. The SEM revealed a significant positive relationship between degree

of activity in the right/left foot region of the somatosensory cortex during simulation and self-reported PSE as measured by the daily diary (path coefficient=0.53). No significant relationship emerged between the right hand and PSE (path coefficient=0.45). Additionally, we see a positive relationship between the degree of activity in the right hand region of the SC during the simulation condition and self-reported AE (path

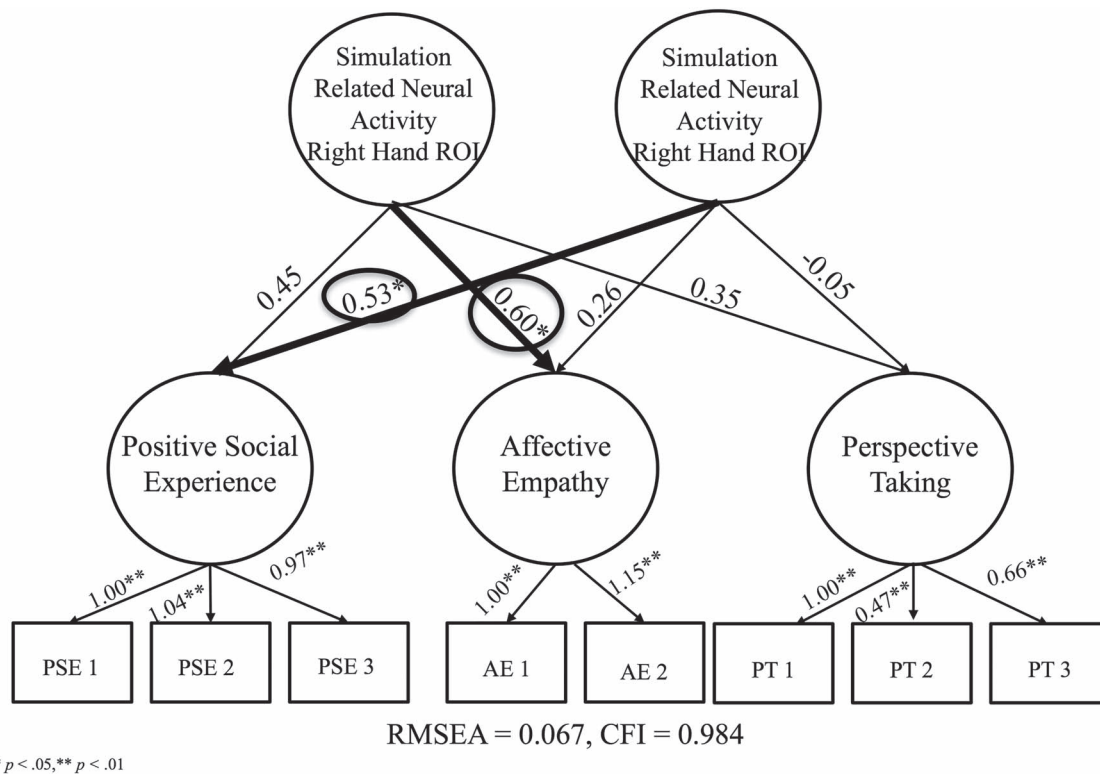


Fig. 3. Structural equation model to model multivariate dependencies between MRI measures and diary constructs. PSE 1—I socialized with other people and I enjoyed it. PSE 2—I socialized with other people, and I look forward to socializing again in the near future. PSE 3—I socialized with other people, and I felt like other people liked me. AE 1—I felt empathy or sympathy for someone else because of their difficult circumstances. AE 2—I had warm, affectionate feelings for someone else. PT 1—I made an effort to understand another person's experience or point of view. PT 2—I tried to imagine what another person might be thinking or feeling. PT 3—I tried to see things from multiple different points of view.

coefficient = 0.60); no significant relationship emerged between the right/left foot and AE (path coefficient = 0.26). There is no significant relationship between the right hand and PT (path coefficient = 0.35) or left/right foot (path coefficient = -0.05).

Subsequently, we performed a *post-hoc* analysis to determine whether the SEM outputs varied between the two groups: CHR vs HC. To test this, we conducted an exploratory multivariate analysis on the data in which the subjects and factor scores (three social functioning constructs: PSE, AE, PT; and two fMRI measures: RH, LRF) were scaled into a 2D space. A principal components analysis was done in order to scale from 5D to 2D, which resulted in the first component explaining 60.35% of the variance, and component two explaining 23.88% of the variance. In a second step, we mapped all subjects in this 2D biplot, and from this, we determined that there is no clear structure allowing us to separate out CHR from HC.

Discussion

This study examined whether brain activity during simulation was prospectively associated with daily social behavior in psychosis-risk and healthy young adults. The present study expands previous literature by investigating the association of simulation-related brain activity with daily reports of real-life social behavior. Three main findings emerged. First, results of the fMRI experiment show evidence of simulation—specifically, our results show that in the absence of visual cues, individuals recruited cortical regions dedicated to somatosensory processing in hand/foot regions when asked to imagine hand/foot

pain. This finding suggests that individuals generated a neural representation of the hand/foot when estimating how they might feel in a scenario in which they experienced hand/foot pain. Second, SEM results showed that simulation-related activity in hand/foot regions of the somatosensory cortex was associated with self-reported AE and PSE across all participants. Third, the amount of simulation-related neural activity as well as the relationship between simulation-related brain activity and social behavior is not significantly different between at-risk and control participants. These results illustrate the neural basis of simulation and suggest that individual differences in simulation are directly related to individual differences in the daily engagement of social processes/behaviors, such as AE, that are putatively reliant on simulation. Together these findings suggest that the capacity and/or use of simulation may explain variation in social functioning in at-risk and healthy populations.

Importantly, this study's novel task design and multi-method approach provided more direct and concrete evidence of simulation than prior investigations. First, the fMRI task was effective in eliciting neural activity associated with the simulation process. Furthermore, by employing an independent functional localizer scan, we identified each person's hand or foot region of the somatosensory cortex; then, we demonstrated specific neural activity in their individually identified hand/foot region during hand/foot-related simulation. This finding indicates that as individuals imagine themselves in a painful situation, they recruit the specific cortical region that is also involved in the physical experience of the imagined situation. This finding is

consistent with previous research highlighting the recruitment of the pain network in healthy adults observing another person in pain (e.g. Singer et al., 2004). Similarly, research on the conceptualization and manipulation of tools also suggests that brain areas typically involved in the experience of using a tool are also recruited when imagining tool use (Wadsworth and Kana, 2011). Together this work suggests that mental imagery of actions and sensations may recruit the same brain regions involved in actual experiences.

The SEM analysis of fMRI and diary data provide evidence that individual differences in neural activation during simulation are associated with real-world social behavior. The diary provides an ecologically valid snapshot of day-to-day functioning. From the diary data, we tested the hypothesis that simulation-related activity is associated with daily social behaviors. As predicted, simulation-related activity in the somatosensory cortex was significantly related to daily reported AE. More specifically, greater levels of neural activity during the simulation task prospectively predicted higher ratings of self-reported AE. This finding is consistent with the idea that embodied simulation, the generation of an internal representation of an emotional experience, may facilitate social cognitive processes like AE. Similarly, simulation-related activity in the somatosensory cortex was significantly related to PSE, such that greater levels of neural activity during the simulation task prospectively predicted greater enjoyment of social interactions over the following week. We did not observe group differences of this brain-behavior (i.e. simulation-related activity to social behavior) relationship; suggesting that the brain-behavior relationship is the same in both at-risk and healthy groups, and that it is likely individual variability within these groups that drives differences in social functioning. The dimensional conceptualization of social behaviors we used in this study allowed us to examine the full range of social functioning, rather than a dichotomous presence or absence of social deficits.

Previous research has looked at the process of simulation in healthy adults, but activation in simulation-related brain regions has not been directly linked with the specific social processes in daily life. Additionally, by investigating this process in a population impaired in social functioning (thereby increasing variability in social functioning in our sample), we are better able to understand how variation in simulation ability might relate to behavior, giving us a broader understanding of the function and importance of simulation in social functioning. The findings from this study suggest that the neural mechanisms linked with simulation may be important for social functioning. The diary approach to assessing social functioning captured individuals' perceptions and experiences of social interaction in a more immediate and personal manner than traditional retrospective reports or clinician-rated assessments. Thus, by directly eliciting and measuring the simulation process, this study provides additional information about the neural mechanisms underlying simulation and its behavioral consequences.

Importantly, recent findings suggest that understanding individual variation in symptoms and outcomes may be central to elucidating the etiology of social behavior deficits in people at psychosis-risk. Collectively, research suggests significant variation in social functioning between individuals across the clinical high-risk spectrum, thus, research focusing exclusively on group differences may not capture the true variance or provide a complete picture. Within the social cognitive and social functioning literature, some CHR individuals may have stronger social cognitive skills than others, thus the group average of

the range of these skills may sum to zero, misrepresenting true individual variability. In a between group study design, this effect could lead to false negative findings. Investigating individual differences in social cognition and behavior may provide important information about the mechanisms of social functioning.

We did not find differences between at-risk and healthy participants in our study. While consistent with some literature (McCormick et al., 2012; Horan et al., 2014; Mukerji et al., 2018), our observation of no simulation-related differences between groups is in contrast with other neuroimaging (Thakkar et al., 2014) and behavioral studies (Schwartz et al., 2006; Matthews et al., 2013) that suggest simulation impairments in individuals with psychotic disorders. There are several possible explanations for these discrepancies. First, in this study, we investigated only one region implicated in mental simulation of pain—the somatosensory cortex. Though we found no group difference in neural activity in this region, it remains unknown whether we might have seen group differences in other simulation-related regions, for example regions involved in mental imagery (e.g. primary visual cortex) and episodic memory (e.g. hippocampus).

Additionally, simulation abilities may co-vary with psychotic symptoms, thus reflecting a difference in simulation abilities across stages of illness. Prior research indicating neural differences in simulation-related processes (Thakkar et al., 2014) as well as behavioral studies of imitation (Park et al., 2008; Matthews et al., 2013) have focused on individuals with schizophrenia diagnoses and these impairments have not been demonstrated in at-risk groups.

Another possible explanation is that simulation processes remain intact when taking the first-person perspective, but fail when taking others' perspectives. Research in schizophrenia suggests that there is a failure of self-other distinctions (van der Weiden et al., 2015)—and separating self from other in third-person PT. It may be that the neural regions involved in differentiating self from other (e.g. medial prefrontal cortex) (van der Weiden et al., 2015) show atypical activity. We hypothesized that individuals recruit the somatosensory cortex during simulation to generate an internal representation of the hand/foot region, but we cannot know for sure what individuals were thinking when asked to imagine the experience in themselves. The fMRI task elicited simulation by asking participants to reflect on the pain experience in their own hand/foot, but not on participants' understanding of another individual's experience. Thus, while simulation of one's own experience should be related to the ability to simulate the experience of another, future work will need to examine simulation mechanisms when thinking about another person's experience.

This study is not without limitations. First, our sample size, particularly for CHR participants, was small and these findings should be replicated with a larger sample. In addition, while the CHR participants had attenuated psychotic symptoms, the symptoms did not occur with the high frequency and recent onset that is required for a psychosis-risk syndrome. Thus, compared to help-seeking or clinic-based CHR samples, our CHR participants may be earlier in the course of illness and/or less impaired by their symptoms—i.e. participant characteristics which could explain the lack of group differences. Similar to other papers investigating simulation (e.g. Jackson et al., 2005), we use a pain paradigm. However, previous literature shows altered pain perception, specifically decreased sensitivity to pain, in individuals with schizophrenia (Singh et al., 2006) and their relatives (Hooley and Delgado, 2001). It is possible that the activity in neural regions involved in the affective and cognitive processes of pain may differ between groups.

Finally, the stimuli in this study were not inherently social. In future work, examining physical social interactions (e.g. hand-shake) or physical emotional responses (e.g. smiling) might provide a closer approximation of simulation in social contexts. We would expect that simulation in social contexts would also be strongly associated with daily social functioning. Moreover, this work examines the simulation process in first-person perspective, recent research suggests that investigating perspective-taking processes during social interactions may offer a unique window into social cognition and functioning (Redcay and Schilbach, 2019).

Simulation is just one of several theories that may explain social cognitive processes and individual variability in social functioning. In this study, we find no group differences in neural activity of simulation-related processes; thus, simulation may not be the mechanism driving impairments in social cognitive processes and social functioning in at-risk individuals. Other processes involved in inferring the mental states of others might better explain these differences. At the same time, we note the relationship between neural activity during simulation and behavioral markers of social functioning, which suggests that simulation-related processes explain individual variability in social behavior. Future studies should investigate other neural processes implicated in the theories of mental state inference, as a more integrative perspective might offer additional explanations.

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Conflict of interest

None declared.

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