Development of Social Cognition in Infants

A Replication Study Using Near Infrared Spectroscopy

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The social brain network has been studied extensively in adults, but the development of this network in infants has received less attention. A relatively new method to measure brain activity in infants is fNIRS. An earlier study used this method to investigate activation in the social brain network of infants, in response to social and nonsocial stimuli. They found localized activation in response to social stimuli. The current study aims to replicate part of this study to increase the reliability of the results and to learn more about the potential of fNIRS in infant studies. A sensor pad with 16 optodes and 22 channels was used to measure the hemodynamic response in infants in response to social dynamic stimuli, nonsocial dynamic stimuli and baseline images. The data of each channel for each infant was inspected and rejected when it did not meet the required criteria. The findings of this study differed from the original study. No support for localized activation in response to social stimuli was found. Possibly this was due to the amount of data that had to be rejected.

Keywords: Social Cognition, fNIRS, Brain Development, Infant Study

Introduction

The network of brain areas involved in social cognition processes, known as the *social brain network* (Adolphs, 2001; Adolphs 2003), has been subject of extensive research, mostly involving adults. The development of these regions in infants, however, has not had the same amount of attention. One of the reasons for the lack of studies to infants' social brain network development is methodological. For example, functional magnetic resonance imaging (fMRI) is mainly used to investigate the activity of these regions in adults, but it remains difficult to study awake and engaged infants with this technique, because the technique requires the participants to remain very still (Wilcox & Biondi, 2015). fMRI studies in infants are therefore usually conducted with sleeping or sedated infants to avoid motion artifacts. This limits the types of experiments that can be done. An alternative to this technique, which is often adopted in infants' studies is electroencephalogram (EEG). The problem with this technique, however, is that it has good temporal resolution, but spatial resolution remains poor (Wilcox & Biondi, 2015; Lloyd-Fox, Blasi & Elwell, 2010).

A study done by Lloyd-Fox and colleagues in 2009 used a relatively new method, known as functional near infrared spectroscopy (fNIRS). This technique has a better temporal resolution than fMRI and allows a more accurate identification of the areas from which cortical responses are obtained than EEG (Wilcox & Biondi, 2015). It can be used on awake and conscious infants, is noninvasive and nonionizing, relatively inexpensive, portable and easy to use (Wilcox & Biondi, 2015). This technique works by sending light from sources on a sensor pad located on the infant's head to detectors. It detects the concentration of oxyhemoglobin (HbO_2) and deoxyhemoglobin (HHb) through changes in attenuation of light. NIRS studies with adults show that HbO_2 and HHb responses are similar to the BOLD fMRI signal changes. However, the pattern is less consistent with infant data (Baird et al., 2002; Meek et al., 1998; Sakatani, Chen, Lichty, Zuo & Wang, 1999; Wilcox, Bortfeld, Woods, Wriuck, & Boas, 2005; Zaramella et al., 2010). It is thus appropriate to investigate both HbO_2 and HHb changes in response to stimuli.

The brain region of interest in the study of Lloyd-Fox and colleagues (2009) was the superior temporal sulcus (STS). This region is part of the social brain network and is considered to work as a biological motion detector, but is also associated with functions like motion in static images, intentionality of action and social relevance of actions (Lloyd-Fox, et al. 2009). They performed two experiments for their research. In the first they used fNIRS to measure brain activity in response to social dynamic stimuli. In the second experiment they also measured brain activity in response to nonsocial dynamic stimuli and compared the two responses. They found that at 5 months of age, infants already have a specialized area of the temporal cortex which is activated by social stimuli. This activation was consistent with the activation in adults, which suggests that infants' functional activation to biological motion perception resembles that of adults'.

Other studies have replicated some of the results found by Lloyd-Fox and colleagues. A study in Gambia measured brain responses to visual and auditory social cues. They found similar localized patterns of activation in response to visual social cues (Lloyd-Fox et al., 2014). Another study that aimed to discover early markers of autism using fNIRS also measure brain responses to visual and auditory social cues. Again similar localized patterns of activation in response to visual social cues was found in infants with low risk for autism. Infants with high risk for autism, however, revealed a different response to both social visual and auditory stimuli (Lloyd-Fox, Blasi, Elwell, Charman, Murphy & Johnson, 2013).

The present research aims to replicate experiment two of the study done by Lloyd-Fox and colleagues (2009). The replication is done to increase the reliability of their results and to learn more about fNIRS and the potential of optical topography as a tool for studying the social brain network in infants. Minor changes in the methodology have been made in this study, which will be expanded upon later. These changes are the result of new insights into the fNIRS system and a different setup. Similar to the original study, this research expects to find that localized activation will occur in response to social stimuli in the posterior half of the sensor pad corresponding to the location of the STS.

Methods

Participants

The study consisted of 8 participants 5 of whom were female (m = 163,2 days, σ = 4,66) and 3 of whom were male (m = 166 days, σ = 7,94. 11 other infants participated, but were excluded from the final analysis as they failed the data rejection criteria (7 infants did not look at the screen for a sufficient amount of time, 5 infants failed the quality assessment of the data). Parents of infants in and near Utrecht were recruited and asked to sign an informed consent form via email. All participants received a present at the end of their visit. The study protocol was approved by the appropriate Ethics Committee.

Stimuli

The stimuli and task used in this replication study are similar to those used in experiment two of the paper by Lloyd-Fox, and colleagues (2009). There are two experimental conditions, social and nonsocial. The social experimental condition consists of social video clips. In these 16s full-color clips female actors, in front of a black background, either moved their eyes left or right, their mouth in silent vowel movements, or performed hand games known as “peek-a-boo” and “incy wincy spider.” These videos had a resolution of 740×549 pixels and each one consisted of two 8s fragments randomly chosen out of a set of six possible fragments. The nonsocial experimental condition consists of nonsocial video clips: moving images of toys, machine cogs and pistons. These videos consisted of four fragments of 4s played in a random order. The baseline condition consists of still images of vehicles (such as cars, helicopters etc.). During the baseline condition eight images were played, which were randomly chosen out of 12 images. The images appeared on screen for an average of 2s.

The participants passively watched these stimuli on a 23-inch screen with a resolution of 1920x1080 pixels, with a viewing distance of approximately 60cm.

Procedure

The parent(s) and their infant were asked to come to the NIRS laboratory at the UMC (University Medical Centre, Utrecht, the Netherlands) to participate in the study. They were informed about the study in detail and asked to hand in the informed

consent (which is normally signed at home, by both parents). The testing started as soon as any further questions from the parent were answered. Any question was answered by the researchers before, during and after testing.

The parent was asked to sit down in front of the screen, with the infant on their lap. A webcam was placed at the top of the screen to record the infant's behavior during the task. The fNIRS headgear was placed on the infant's head by one of the experimenters while the other distracted the infants. A picture of the band position was taken before the task began. This was done so it could later be checked if the headgear was placed in the correct position. Another headband was placed over the fNIRS headgear, to prevent the infant from touching and pulling the wires. After the end of the task the researchers took a note about the position of the band (same or different position compared to the beginning of the task). If the headgear had shifted too much the data became unreliable.

The social movement task began after the lights were turned off. The stimulus presentation started with a rest period during which the infant was shown shapes in the four corners of the screen to familiarize them with the general setup of the experiment. A 16s experimental trial (social or nonsocial video) was followed by a 16s baseline trial (still image of a vehicle). After the baseline the second experimental trial (social or nonsocial) played for 16s. This order was repeated twice before being interrupted by a preferential looking trial that lasted 5s. This trial consisted of the simultaneous presentation of a social still image and a nonsocial still image, one on the left and one on the right side of the screen. After 6 more trials there was another preferential looking trial in which the social and baseline images were displayed on the opposite side of the screen. In other words, if the social stimulus appeared on the right side of the screen during the first preferential looking trial, it would appear on the left side of the screen during the second preferential looking trial. Thereafter, the two experimental and the baseline trial continued to be displayed until the infant became bored or fussy for a maximum of 5 minutes. When necessary the researcher could play an alerting sound in between the trials to bring the infant's attention back to the screen, see figure 1 for the timeline of the experiment.

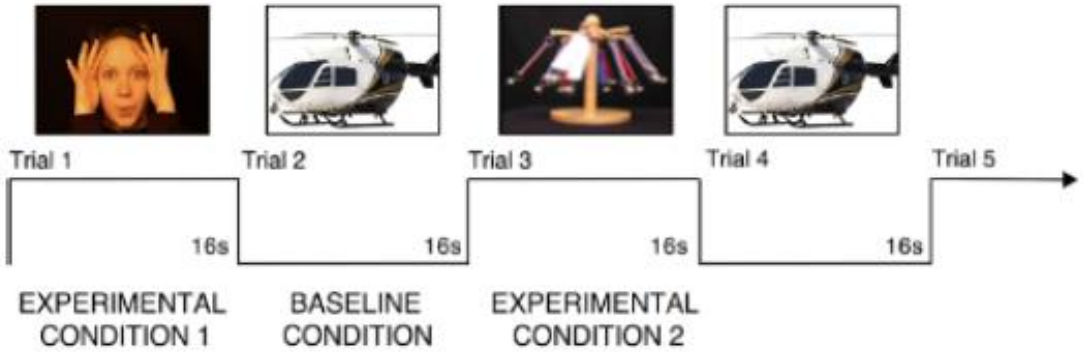

Figure 1. Procedure experiment. The experiment started with either a social or nonsocial experimental trial. There were a maximum of 10 trials for each experimental condition, but the experiment was stopped if the child became fussy. Image used from Lloyd-Fox et al. (2009).

Data acquisition

fNIRS measurements were made with the UCL topography system, a multichannel system that uses two wavelengths at 780 and 850nm in a frequency multiplex approach allowing rapid data acquisition of the attenuation signal from the reflected near infrared light. Unlike Lloyd-Fox and colleagues' work this study used 16 optodes, in a 22-channel arrangement with an inter-optode separation of 20mm, placed on the right temporal lobe, see figure 2. The headgear was placed over the right hemisphere and aligned parallel to the eyebrows with channel D5 aligned perpendicular to the ear point. This way the posterior area of the pad lies approximately over the scalp locations T5/6, analogous to the region of interest (STS).

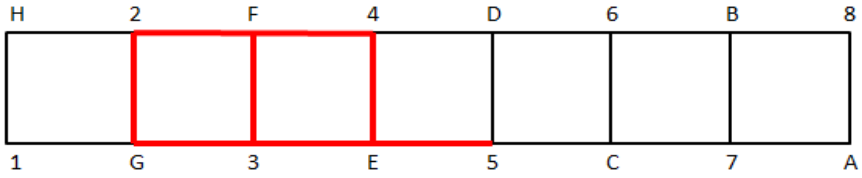

Figure 2. Scheme of the optode and channel arrangement as used at University Utrecht. Letters represent sources and numbers represent detectors. The red lines mark the area of interest located above the STS. Separation between sources and detectors is 2cm.

Data rejection

The selection criteria for valid trials were slightly different than the ones used by Lloyd-Fox and colleagues (2009). The percentage of time the infant was looking at the screen was recorded and coded after the experiment. An experimental trial was valid when the child was looking at the screen for a minimum of 60% of the trial, and

30% of the preceding baseline trial. The first experimental trial was not preceded by a baseline trial, and was thus considered valid if their looking time was at least 60%. The original study used 80% as its cut-off point for the experimental trials. The old criteria was adjusted in later papers, because too many trials had to be rejected. A minimum of 3 valid experimental trials for each condition were required to include an infant in the study. In the original study a minimum of valid experimental trials was 6, but this number was changed to include more infants. After the selection for looking percentage 13 of the original 20 infants tested remained.

The data of the 13 infants that were left after the first selection was then assessed and trials or channels were rejected from further analysis based on the quality of the signals. This was done manually to save more channels compared to an automatic channel rejection procedure. To begin, the data before the start and after the end of the task were excluded. Time windows in which there was a very high peak that matched a clear movement observed in the recorded videos were first marked. The channels were then inspected visually one by one and channels with excessive noise were excluded from further analysis. Noise was considered excessive if intensity of the light is too low, lower than 0.05 for >50% of the trials, or too high, higher than 0.8 for >50% of the trials. Channels were also excluded if the change in intensity of the light is too high, this means when peak-to-peak amplitude is >0.1 for more than 5 times during the trials, the peaks caused by movements that were marked previously were not considered in this count. Lastly the power spectral density was checked for each channel. If there was a peak around 2Hz, the channel was not pruned. This peak at 2Hz indicates that the system detected the heartrate of the infant.

There were 8 infants who had at least 50% of the channels passing the manual quality assessment at least one of which was located over the region of interest of the task (occipital/temporal). The data from the other 5 infants were rejected from further analysis.

For the detection and correction of any remaining motion artifacts two functions were used. Wavelet motion correction and motion artifact by channel (Brigadoi et al. 2014; Cooper et al. 2012). Both work on change in optical density (OD) data. Wavelet motion correction performs motion artifact detection and then corrects them. Motion artifact by channel detects the motion artifacts, but does not correct them. First wavelet motion correction was applied and then motion artifact by

channel was applied to see if there were still any parts of the signal detected as a motion artifact. When motion artifacts corrupted more than 50% of the experimental trial, it was rejected. There was no trial corrupted for more than 50%, thus none of the 8 remaining participants were rejected.

These signal processing steps are required to extract useable data on hemodynamic changes and are based on the processing steps typically executed in NIRS studies (Lloyd-Fox, Blasi & Elwell, 2010). The original study by Lloyd-Fox and colleagues (2009) generally followed the same steps, but quality assessment was done automatically.

Analyses

For the analysis Homer2 (homer-fnirs.org) was used. The data was converted from optical density units into changes in concentration of HbO_2 and HHb using the modified Beer-Lambert law. Valid experimental stimulus trials were averaged together for each infant over the time period of 4 seconds before the onset of the experimental trial until 35s after the trial ended. A time course of the mean change in HbO_2 and HHb was plotted for each channel (across all infants). This made it possible to visually examine the complete hemodynamic response course until the point it turned back to baseline.

As in the study by Lloyd-Fox and colleagues (2009) a time window was selected between 10 and 18s post stimulus onset. This period of time was selected to include the range of maximum changes observed across infants for HbO_2 and HHb. Statistical comparisons of the response to experimental versus baseline trials across all infants were made using the valid data for each channel. A paired *t* test was performed during the specified experimental trials time window to compare the maximum change in HbO_2 and HHb with the mean of the baseline trial. Another paired *t* test was performed in each channel to compare the activation in response to the two different conditions.

Results

After applying the selection criteria described above, valid data were obtained from 8 of the 20 infants tested. The proportion of valid channels across the group of infants that were included was 74,7%.

In the first step of the analysis it was determined which channels were activated upon watching the social and nonsocial videos. A paired *t* test of the maximum increase (or amplitude) in HbO_2 in response to the social dynamic experimental condition (during the specified time window of 10-19s poststimulus onset) revealed a significant increase from the baseline in HbO_2 in one channel (Channel C6: t = -2.856, p = .025, df = 7; note that the degrees of freedom depend on in how many infants recordings were achieved for those channels). This channel was located outside of the area of interest.

There were also significant changes in the concentration of HHb across infants in four channels (Channel C5: t = -5.098, p = .004, df = 5; Channel C6: t = -3.556, p = .009, df = 7; Channel E5: t = -4.664, p = .004, df = 6; Channel G1: t = 4.944, p = .004, df = 5). Channel E5 was located in the area of interest, over the location of the STS. The other three channels were located outside the area of interest.

A paired *t* test of the maximum increase (or amplitude) in HbO_2 in response to the social dynamic experimental condition revealed a significant increase from the baseline in HbO_2 in two channels (Channel F2: t = -4.230, p = .008, df = 5; Channel F3: t = -3.280, p = .031, df = 4). Both are located in the area of interest. There was also a channel which showed a significant change in the concentration of HHb across infants (Channel E3: t = 5.753, p = .004, df = 4). This channel is also located in the area of interest.

It was then determined whether there was a difference in activation in response between the two different channels. A paired *t* test to compare the difference in maximum increase in HbO_2 from baseline during each experimental condition revealed a significant difference between the response for the social dynamic and the nonsocial dynamic stimuli in two channels (Channel B7: t = -2.737, p = .041, df = 5; Channel E5: t = 2.578, p = .042, df = 6). Channel B7 showed a significantly larger increase in HbO_2 in response to nonsocial dynamic stimuli. Channel E5 on the other hand showed a significantly larger increase in HbO_2 in response to the social dynamic stimuli. The latter channel is located in the area of interest.

There was also a significant difference in maximum increase in HHb from baseline between the response for the social dynamic and nonsocial dynamic stimuli in one channel (Channel E5: t = 4.213, p = .006, df = 6). Channel E5 shows a

significant larger increase in HHb concentration in response to the social dynamic stimuli, in the area of interest (as mentioned earlier).

Table 1
Channels with significant changes in HbO_2 and HHb concentration

Social dynamic experimental condition (paired t-test)			
HbO2		HHb	
Channel	*p*	Channel	*p*
C6	.025	C5	.004
		C6	.009
		E5	.004
		G1	.004

Nonsocial dynamic experimental condition (paired t-test)			
HbO2		HHb	
Channel	*p*	Channel	*p*
F2	.008	E3	.004
F3	.031		

Social dynamic vs nonsocial dynamic experimental condition (paired t-test)			
HbO2		HHb	
Channel	*p*	Channel	*p*
B7	.041	E5	.006
E5	.042		

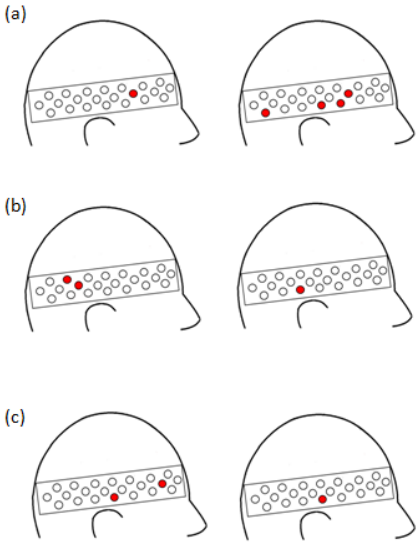

Figure 3. Channels with significant changes in HbO_2 concentration (left) and HHb concentration (right). (a) social dynamic; (b) nonsocial dynamic; (c) social dynamic vs nonsocial dynamic.

Discussion

The findings of the experiment differed from those made by Lloyd-Fox and colleagues (2009). The original study found that there were significant hemodynamic increases in HbO_2 in response to the social dynamic stimuli on scalp locations T5 and T6, which correspond to the STS. Furthermore they found no significant HbO_2 concentration changes in this area in response to the nonsocial dynamic stimuli.

In this study, however, there were no channels with a significant increase in HbO_2 in response to the social dynamic stimuli in the area of interest. The current experiment did however find two channels with a significant change in

HbO_2 concentration in response to the nonsocial dynamic stimuli in the area corresponding to the STS.

Lloyd-Fox and colleagues (2009) also reported no significant increases in HHb concentration in response to the social dynamic stimuli or nonsocial dynamic stimuli. In this study a significant increase in HHb concentration was found in response to the social stimuli in one channel in the area of interest. In response to the nonsocial stimuli three channels in the area of interest showed significant HHb concentration changes.

When directly comparing the response to the social stimuli with the response to the nonsocial stimuli Lloyd-Fox and colleagues (2009) found that the social stimuli had a significantly greater increase in HbO_2 compared to the nonsocial stimuli in the posterior channels of the pads near scalp locations T5 and T6. This study also found a channel with greater increase in HbO_2 in response to the social stimuli compared to the nonsocial stimuli in the region above the STS. However, this study also found that the increase in HHb concentration in that same channel was greater in response to the nonsocial stimuli compared to the social stimuli.

The findings in this study would thus disprove the hypothesis that localized activation occurs in response to social stimuli in the area of the sensor pad corresponding to the location of the STS. This is also in contrast with the results from the fNIRS study in Gambia and the fNIRS study on infants with low and high risk of autism (Lloyd-Fox et al. 2014; Lloyd-Fox, Blasi, Elwell, Charman, Murphy & Johnson, 2013).

There were problems with the data in this experiment that could explain why the results differ from those in the other studies. Even when the quality check of the data was done manually a lot of channels had to be removed. Only 8 of the 20 infants had sufficient clean data to be used in further analysis. In comparison, the study by Lloyd-Fox and colleagues (2009) had useable data from 12 of the 19 infants that participated.

As mentioned before, the pattern of HbO_2 and HHb responses in infant data is less consistent than in adults. Changes in HbO_2 are generally consistent across infant studies and similar to that observed in adults. HHb results on the other hand are far less consistent in infants (Lloyd-Fox, Blasi & Elwell, 2010). This could explain why

in this study changes in concentration of HHb are found whereas the study by Lloyd-Fox and colleagues reports no changes.

Beside the activation in the area of the pad corresponding to the STS there were some channels with significant increase in HbO_2 and HHb concentration in response to social stimuli in the more anterior region of the sensor pad. Similar findings were reported in the original study. An explanation is offered in a study by Imaruoka, Saiki and Miyauchi (2005), who found that anterior regions of the brain are involved in object representation in visual working memory.

In sum, contrary to what was expected this research did not find similar patterns of activation as the study by Lloyd-Fox and colleagues (2009). More data should be gathered or quality assessment should be adjusted before conclusion can be made about the reliability of the original study.

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