Hesitations and intentions in action

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Our experiment will assess the respective role of the mirror neuron system (MNS) and theory of mind areas for understanding someone else*s immediate intentions and state of mind (prior intention). We want to test the hypothesis that making...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Psychiatric disorders NEC
Study type	Observational non invasive

Summary

ID

NL-OMON37077

Source
ToetsingOnline

Brief title
Intentions in action

Condition

- Psychiatric disorders NEC

Synonym
Autism

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: NWO;HCMI nr. 10-43,Hersenstichting Nederland;nr 2010(1)-29

Intervention

Keyword: Autism, Functional magnetic resonance, imaging, Social cognition

Outcome measures

Primary outcome

The dependent variables are the number of correct answers, the response latency

or looking time of the subjects, and, for the fMRI data, the percent signal

change in every voxel of the brain during performance to the tasks.

Secondary outcome

n.v.t.

Study description

Background summary

We are able to recognize/understand someone else's believes, states of mind, and intentions. This ability grossly subsumed under the label 'mentalizing' (forming a Theory of Mind) is thought to form the core of our social skills. Previous studies have found that autistic individuals often have difficulties in tasks requiring to understand the believes of someone else (typically, false believes tasks). This is probably one of the most common deficits found in the autistic population along with poor eye contact and stereotyped repetitive behaviours. However, the late achievement of this skill in the healthy population, around 4 years old, does not match the early time course of autistic symptoms. The origin of the difficulty understanding other people must lie somewhere else, in a skill that autistic children fail to develop between 1 and 2 year-old. One hypothesis is that a deficit of the mirror neuron system could be involved at an early stage of the pathology.

Mirror neurons are neurons from the ventral pre-motor (vPM) and inferior parietal (IP) cortex that fire both during the execution of an action and during the observation of a similar action performed by someone else. Neurons with such mirroring property would enable the observer to enact the action that was witnessed, and through this process plainly understand its goal. Evidence from intracranial recording in the monkey actually suggests that the MNS does not merely encode the kinematics of the action performed by someone else, but the immediate goal of the action. In fact, mirror neurons do fire even when the last part of the action (the grasp itself) is not visible. Finally, mirror neurons also fire to the sound that results from a common action being performed by someone else.
Some experiments even suggest that mirror neurons could play a role

beyond the mere comprehension of the immediate goal of the action, in understanding the state of mind and the believes of the agent. The results of one experiment in humans for instance suggest that the activity of the vPMC is modulated by the context of the action (witnessing someone grasping a cup for drinking activated the vPMC more than viewing the same action in the context of cleaning up the table).
Evidence of a dysfunction of the MNS in autism is meagre. A couple of studies have found abnormalities in MNS functioning, but others have stressed the fact that autistic individuals do not show the expected profile of performance of someone with a MNS deficit. In particular, autistic individuals are quite able to imitate and to learn by imitation, they sometimes demonstrate echolalia (repeating what they heard word-by-word with little comprehension), and may develop exceptional manual abilities (like sculpture, craft, drawing, or the ability to play music instruments).
On the other hand the hypothesis that the MNS could by it-self serve the comprehension of higher levels of intentions, believes, and states of minds has also been criticized. One possibility however is that of a collaboration between the MNS and the medial prefrontal cortex (MPFC), an area that plays a central role in thinking about self and others.
Our study is designed to explore the relationships between the MNS and the MPFC which we suspect are disturbed in autism spectrum disorders.

Study objective

Our experiment will assess the respective role of the mirror neuron system (MNS) and theory of mind areas for understanding someone else*s immediate intentions and state of mind (prior intention). We want to test the hypothesis that making inferences about the prior intentions of someone on the basis of the kinematics of the action of the person requires a collaboration between the vPMC (MNS) and the MPFC (Theory of Mind area). In contrast, making inferences about the immediate goal of the action of someone is not supposed to require the intervention of theory of mind areas. The mirror neuron system is likely to be sufficient to understand the immediate intention of the actor, even when the goal of the action is out of sight. We ought to show that autistic individuals demonstrate preserved activation of the mirror neuron system during processing of immediate intentions, but that the pattern of connectivity between vPMC and MPFC during processing of prior intentions is disrupted, and the degree of disruption at this level correlates with the performance of the patient in theory of mind tasks and perspective taking.

Study design

For the present study we have built an original set of stimuli that can be used to investigate both the process of understanding someone else's intentions in action, and states of mind. The stimuli are movies of an actor picking a ball inside a box.

The actor sits behind a table. Only the torso is visible; the head is outside the field of view of the camera. The camera shows the hand of the actor until it disappears inside the box. There are always 2 balls inside the box; one big and one small ball. The two balls always have different colors and different saturations. On some occasions the actor was told which ball to pick (the big or the small one). On other occasions the actor was asked to select the less saturated ball. In this later condition, the actor was likely to hesitate. Some of these hesitations are indeed very obvious, even on a 2-second movie. Witnessing an hesitation gives a direct information about the state of mind of the agent.

Twelve actors were involved in the creation of the stimuli, mostly colleagues and family members. All the actors were explained the experiment and signed an informed consent. The actors recruited are between 6 and 55 year-old, half of them are males. We decided to include actors from different ages and gender in order to increase (1) the diversity of the kinematics -and therefore the demand on the simulation mechanism (MNS), and (2) the diversity of the characters -and therefore any demand on the mechanism of perspective taking (Theory of Mind).

The same movies can be the object of different questions: One that taps the MNS (e.g. Does s/he pick the big or the small ball?), one that requires mentalizing (e.g. Was s/he asked to pick the less saturated ball?), and two control questions, one of disposition attribution (e.g., Is s/he a very smart person?), and one low level visual condition (e.g. Is the tip of the chin visible on the video?). Two additional sets of movies were also taken with every actor for use as control conditions. One series of movies show the actors performing a non-meaningful gesture above the box (meaningless gestures condition), and one series of movies show the actor picking a ball on the table with the box on the side (full-vision condition). This last condition will permit to control for possible differences with previous studies where the goal of the action is always visible.

During the fMRI experiment, both autistic and control participants will perform a number of different tasks while their cerebral activity is recorded in a 3.0T scanner with standard image acquisition parameters.

1. Execution task
One task is the execution of grasping movements. The results of this task will be used to delineate the brain regions involved in motor execution of grasping action. It is a standard procedure to delineate the plausible location of the MNS. The participants will be requested to pick a ball next to them when they hear a tone, and to put it back before the next tone (8 sec later). There are two different tones. Upon hearing a low tone the participant will be requested to pick the ball on the left, and upon hearing the high tone s/he will pick the ball on the right. Participants will pick 15 times a ball on each side. Items are separated by a 12 sec rest period. A total of 120 brain volumes will be acquired during a single 11-min EPI sequence.

2. Theory of Mind task
Another task will be used to localize brain areas involved in theory of mind reasoning. In this task, participants will read 24 short narratives about the formation of a representation (12 about beliefs, 12 about physical representations like a photo, drawing, or map) that do not correspond to reality. Stories are on average 32 words long, and are presented for 10s. Participants then answer a fill-in-the-blank question about the representation (presented for 4 s). Stories of the two conditions alternate with a 15-s rest period after each story. Participants will perform two 6-min runs of this experiment (12 stories each).

3. Action monitoring
In order to identify brain areas involved in action monitoring participants will be given another localizer. In this experiment participants will perform a numerical interference task in which they have to indicate the largest of two numbers that vary in size. Incongruents items (e.g. with the larger number displayed in smaller font) are mixed with congruent items. Items are presented in blocks of 5 (with one item every 2.5 s) and the participant answer by pressing one of two keys corresponding to the side of the response. In a control condition, letter-number pairs are displayed on the screen and the participants must indicate the side of the letter. The timing of the stimuli is the same as for the main condition. Blocks of the 2 conditions alternate and are separated by a 12-s rest period. Participants will perform two 6-min runs of this experiment (12 block of each condition).

4. Observation tasks
Finally, in the main task, participants will observe grasping movements and non-meaningful gestures and will answer different questions about the items. Items last for 12 sec and are composed of 6 movie clips (about 1.5 s each) separated by a cross. The same actor is depicted performing a grasping or a non-meaningful action in the 6 clips. Items are preceded by a one-word question and the participant must answer after the 6 movies (in order to model-out the cerebral activity related to the key press and the instruction). There are 6 different conditions:

C1: Attribution of prior intention / state of mind (Did s/he had to choose the less saturated ball at least 3 times or not?)
C2: Attribution of immediate intention (Does s/he pick the big ball at least 3 times or not?)
C3: Attribution of dispositional state (Is s/he a very smart person or not? - or is s/he very self-confident or not?)
C4: Visual control (Is the tip of the chin visible on the video at least 3 times?)
C5: Meaningless (Does s/he touches the box at least three times or not?)
C6: Full-vision control (Does s/he pick the big ball at least 3 times or not?)

The order of condition is randomized. There are 12 items per condition (72

brain volumes), and the number of yes and no responses is fairly distributed across conditions. Every item will be followed by a 10-sec rest period. Images of the whole brain will be acquired across 3 runs (12 min each). Before starting the experiment, the participants will view a few un-cut movies presenting the complete grasping action performed by the actors, and will be given the opportunity to manipulate a ball of each size. In addition, the participants will perform a few trials of the tasks.

The action observation, action execution, action monitoring, and theory of mind conditions will be tested in separate runs to avoid inflating the variance of error in the cognitive conditions. A full brain anatomical scan will be acquired in every participant for rendering of the activation maps, as well as a short anatomy (with the same number of slices and dimension as the EPI functional runs) for realignment purposes. Finally, diffusion tensor images will be acquired for analysis of the integrity of the white-matter cortical tracks. The total duration of the MRI experiment is 85 minutes. On a separate session, the participants will perform additional tests of Theory of Mind functioning, as well as an IQ test (see below).

Behavioral tests
In the behavioral tests, participants will view the same short movies with different actors picking balls inside the box. They will have to judge the size of the ball being picked, to detect the hesitations of the actor, to judge the jerkiness of the movement. Later they will also be asked to evaluate the self-confidence or self-esteem of the actor on a 5-point scale. The 12 actors are shown separately. There are 12 movies per actor. The items and the conditions are mixed pseudo-randomly. Responses and latencies are recorded by the computer. Participants will be given the IRI empathy scale for correlation with their behavioral performance, and handedness will be assessed with the Edinburgh inventory. Results to the tests will be used for the analysis of the fMRI data in order to identify the effect of different dimensions of the stimuli on the cerebral activity. The total duration of the session is approximately an hour.

Study burden and risks

BURDEN: The burden associated with the cognitive tests is minimal. Short breaks will be inserted between the tasks at the request of the participant, or if the experimenter feels it is necessary.
For the MRI, the burden is obviously higher since participants have to lie still in a confined space while performing the task. However our experience is that most participants with or without ASD can easily make it, and are very glad to participate. We kept the total duration of the MRI scan under one and a half hour in order to minimize the burden. In addition, after 45 minutes, the participant will be asked if s/he requires a 5-min break.

RISK: The experiments will not entail more than minimal risk to the

participants.

BENEFIT: The study is not intended to benefit the subjects directly. However, the data collected during this study could improve our understanding of autism and human cognition at large. In particular, this investigation could help us clarify why autistic individuals are unable to recognize the state of mind of someone else.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• Healthy individuals with normal IQ and normal or corrected to normal vision.
• Between 18 and 55 y.-o.
• DSM-IV diagnosis of Autism Spectrum Disorder, and above cut-off scores on the ADOS for

participants in the ASD groups.

Exclusion criteria

For both the MRI and the behavioural testing:
• Neurological problems (including epilepsy)
• Use of drugs
For the MRI:
• MR incompatible implants in the body
• Any risk of having metal particles in the eyes
• Tattoos containing red pigments
• (Suspected) Pregnancy
• Claustrophobia
• The refusal to be informed of structural brain abnormalities that could be detected during the experiment

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	30-06-2008
Enrollment:	135
Type:	Actual

Ethics review

Approved WMO Date:	07-10-2008
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	20-02-2009
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	08-03-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL21791.042.08