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Organizing events in time and space: one or two impairments in patients with schizophrenia ?

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Schizophrenia

Schizophrenia is a very invalidating pathology affecting about 1% of the population.

Main symptoms are delusions, hallucinations, autistic withdrawal, and disorganization of thought, i.e. fragmentation of consciousness and behavior.



Schizophrenia

Many cognitive functions are also altered.

But how do they relate with one another and with clinical symptoms?



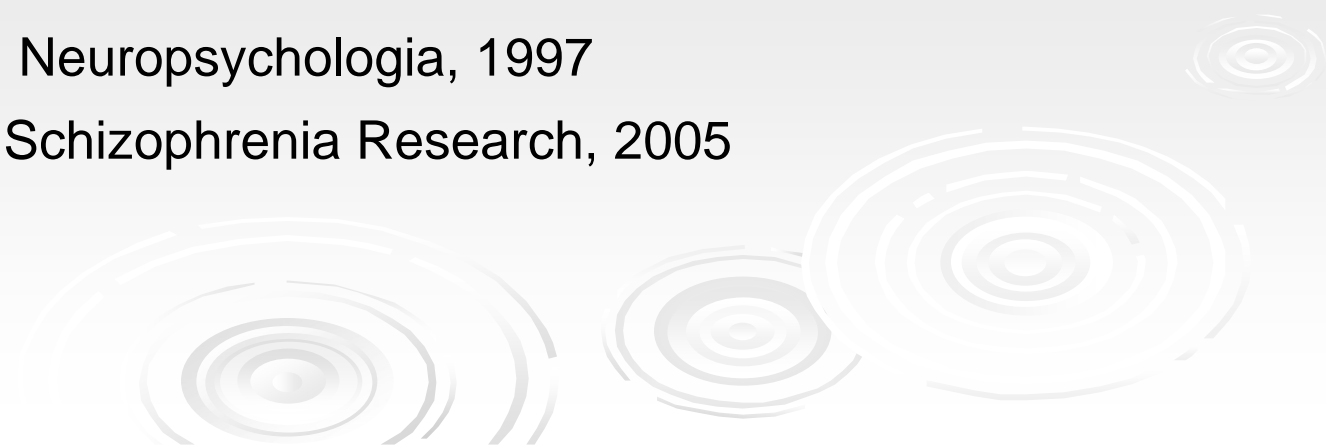
Schizophrenia

Psychiatrists have tried to relate clinical disorganization with some impairments observed in different cognitive domains.

Visual perception impairments have been related to disorganization.

Phillips & David, Neuropsychologia, 1997

Minassian et al, Schizophrenia Research, 2005



Schizophrenia

Thought is also disorganized in time.

Among different symptoms, the sense of time continuity has been described as (clinically) disrupted in patients with schizophrenia (Fuchs, 2007).

Our results support experimentally the idea of an impaired sense of continuity.

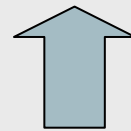
Schizophrenia

This leads to the question of the relationships between these different impairments.

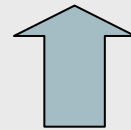


Schizophrenia

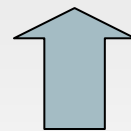
Clinical symptoms (Clinical disorganization)



Secondary cognitive impairments



Primary cognitive impairment(s)



Neurobiological impairments



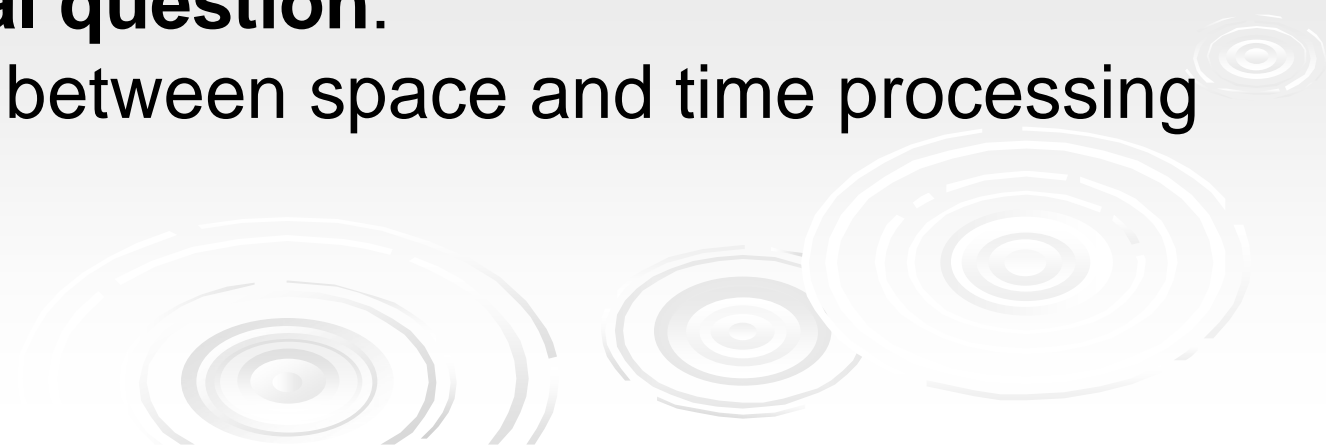
Schizophrenia

Applied question:

Is there one or several fundamental impairments that originate secondary cognitive impairments, underlie clinical symptoms, and should be targeted with new therapeutics?

Fundamental question:

Relationship between space and time processing



Plan

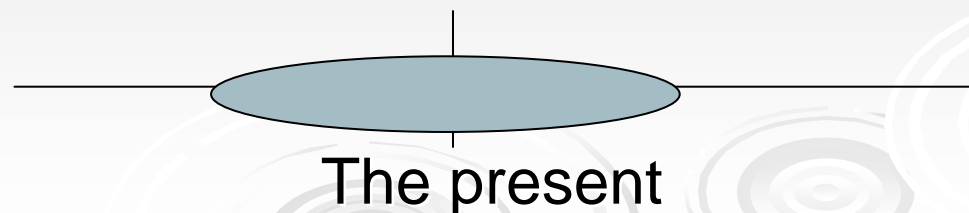
- Time events organization
- Visual organization
- Preliminary results regarding the relationship between time and visual organization impairments.



The concept of temporal window can be related with the sense of continuity

Husserl said that the sense of time continuity relies on the integration of past, present and future moments.

Since moments are integrated, present time is not a single point on the time scale, but has a duration. At a neuronal level, coding an event also requires time, and different events overlap.



- ❖ Many studies have suggested that patients have a difficulty to discriminate time durations (Davalos et al, *J Neuropsychiatry Clin Neurosci* 2005; Elvevåg et al *J Abn Psychol* 2004; Haggard et al, *NeuroReport* 2003; Volz et al, *NeuroReport* 2001)
- ❖ Our question concerned more elementary aspects of time perception, related with the sense of time continuity.



We explored the ability to discriminate synchronous from asynchronous stimuli.

Demo


A decorative graphic at the bottom of the slide consisting of several sets of concentric circles in shades of gray, resembling ripples in water. One set is large and centered, with two smaller sets to its left and right, and a tiny set in the upper right corner.

- Subjects usually judge stimuli as synchronous even if there is a SOA of up to 50 ms between the stimuli:

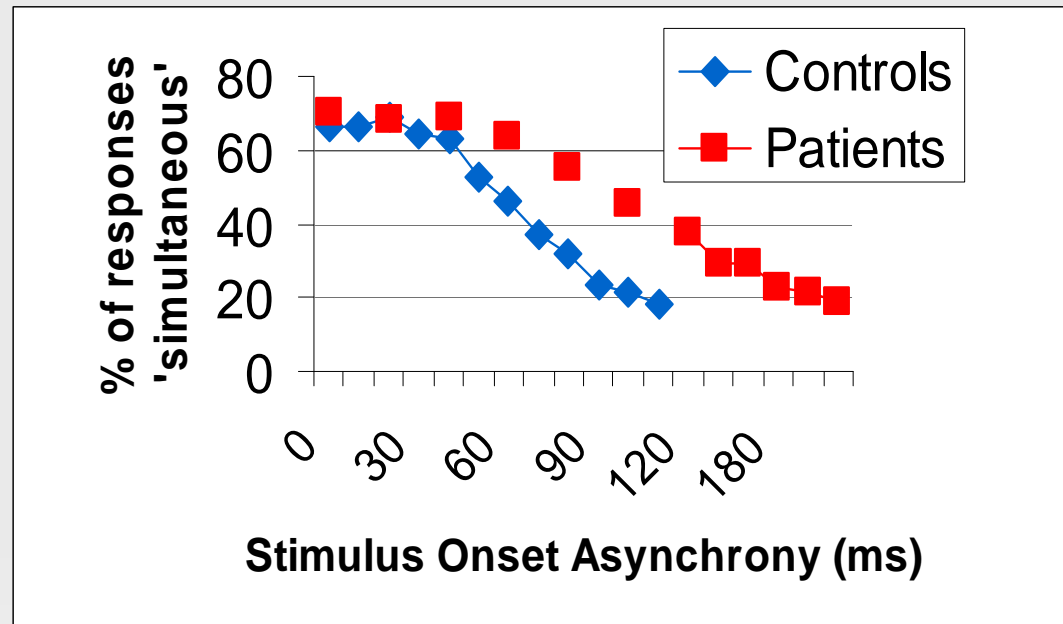
Consistent with the idea that coding an event takes time and that successive events overlap in time.



19 stabilized patients vs 19 matched controls

- AGE Patients: 30.6 – Controls: 30.1 years
 - Education level: 13.2 in patients vs 13.2 years in controls
 - Patients are treated with atypical neuroleptics: Chlorpromazine equiv. 243
 - PANSS = 75.4 (positive 17.5; negative 21.2; global 36.7)
- 

In order to check for bias effects we used a priming effect and distractors, and the experiment was rather difficult. The difficulty amplified the alteration.



N=19 in
each group

Threshold: 60 ms 110 ms

The quality of the psychometric curve allows to eliminate an explanation in terms of a trivial attention deficit.

We checked for bias effects

- Signal detection theory
- Priming effect.

And for the role of distractors

The thresholds still differ in patients and controls in the absence of distractors (Foucher et al, Schizophrenia Research, 2008; Giersch et al, Schizophrenia Bulletin, 2009).

Since then, similar results have been observed in first-episode patients (Schmidt et al, proceedings of the Fechner Day 2009).

This means that

- Patients have a difficulty to discriminate events in time at least at a subjective level.



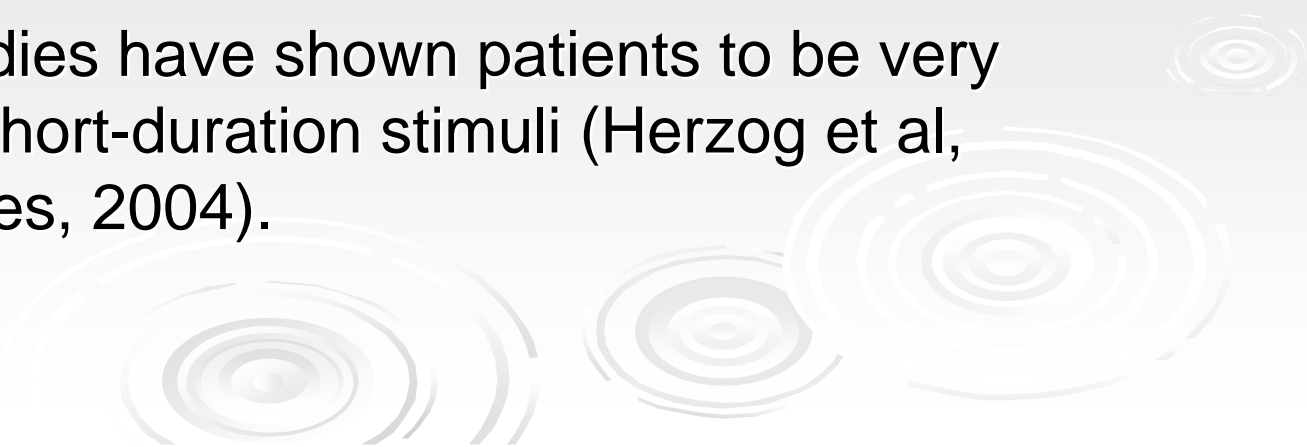
Next questions were

Is there an impairment also at a subconscious level?

Does it mean that patients bind events together when they fall within the same temporal window?

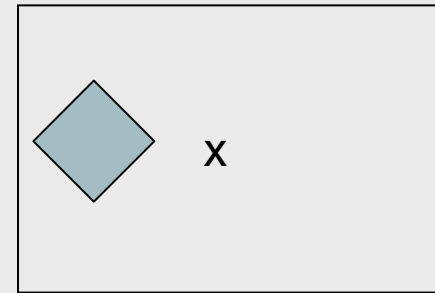
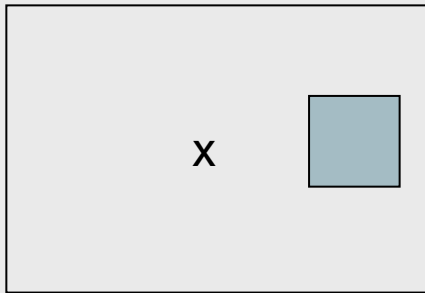
This would contrast with visual perception, for which studies rather suggest a bias toward local details.

Previous studies have shown patients to be very sensitive to short-duration stimuli (Herzog et al, Psychiatry Res, 2004).



To address this question

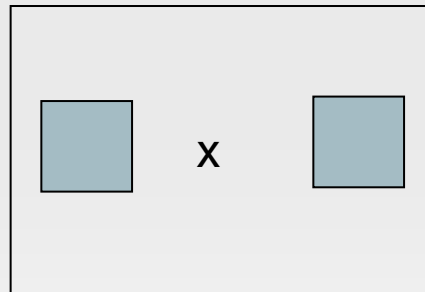
- We took advantage of the Simon effect:



RTs are faster when the stimulus and the response are on the same side rather than on opposite sides

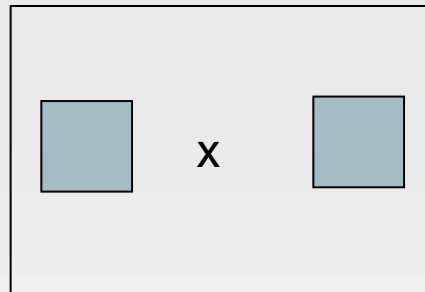
When there is two squares displayed in succession

If subjects attend to the two squares, this should lead to an expectancy regarding the second square and a sense of direction. Hence, there should be a Simon effect on the side of the 2d square.



When there is two squares displayed in succession

In contrast, if patients separate events and are sensitive to short-duration events, their response might be biased by the 1st square.



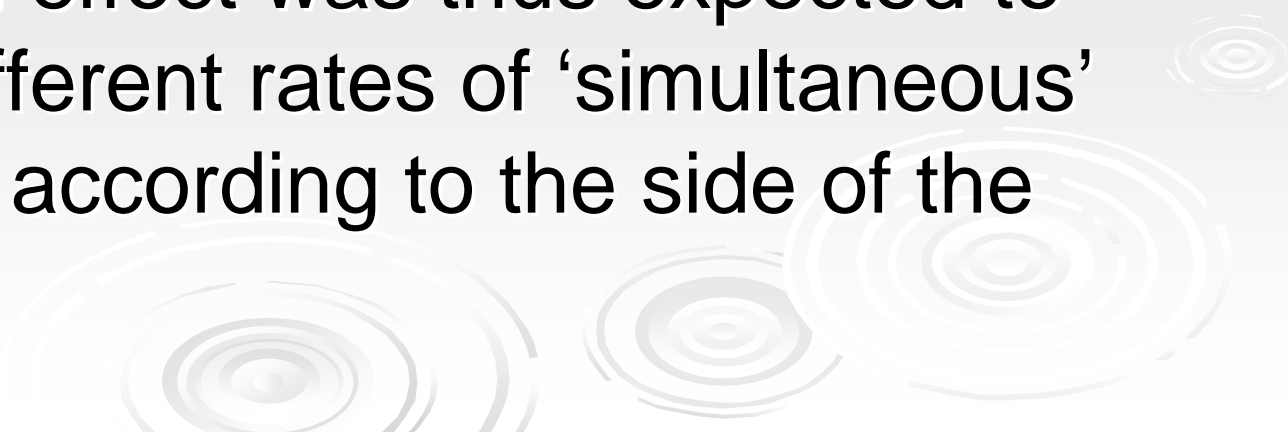
When there is two squares displayed in succession

displayed in succession


In case of synchrony, there should be no Simon effect.



In our experiment,

- The left response key was associated with the response 'simultaneous'.
 - The right response key was associated with the response 'asynchronous'.
 - The Simon effect was thus expected to result in different rates of 'simultaneous' responses according to the side of the squares.
- 

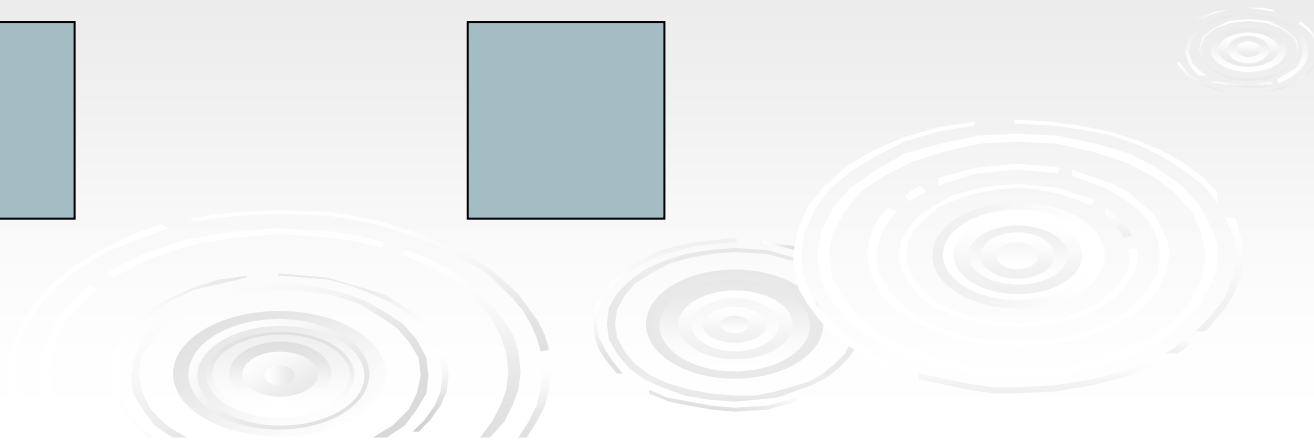
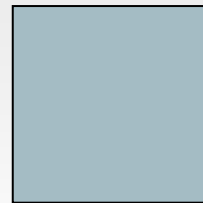
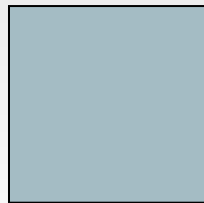
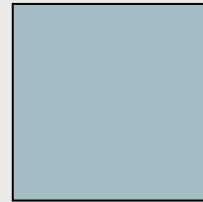
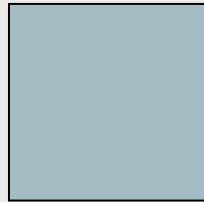
18 stabilized patients vs 18 matched controls

- AGE Patients: 35.7 – Controls: 34.3 years
 - Education level: 11.8 in patients vs 12.5 years in controls
 - Patients are treated with atypical neuroleptics: Chlorpromazine equiv. 259
 - PANSS = 70.3 (positive 15; negative 19; global 35.8)
 - One patient is not treated.
- 

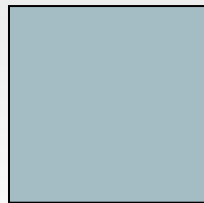
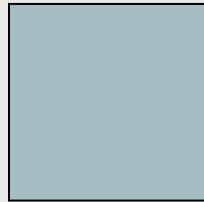
- Threshold in controls: 41.7 ms
- Threshold in patients: 50.1 ms



- The paradigm allowed to check for the possibility of an impairment regarding the Simon effect itself.

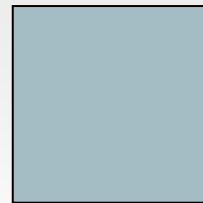


- The paradigm allowed to check for the possibility of an impairment regarding the Simon effect itself.



Left intra-hemifield presentation

- The paradigm allowed to check for the possibility of an impairment regarding the Simon effect itself.



Right intra-hemifield presentation

- Continuous eye-tracking ensured that subjects looked at the fixation point.

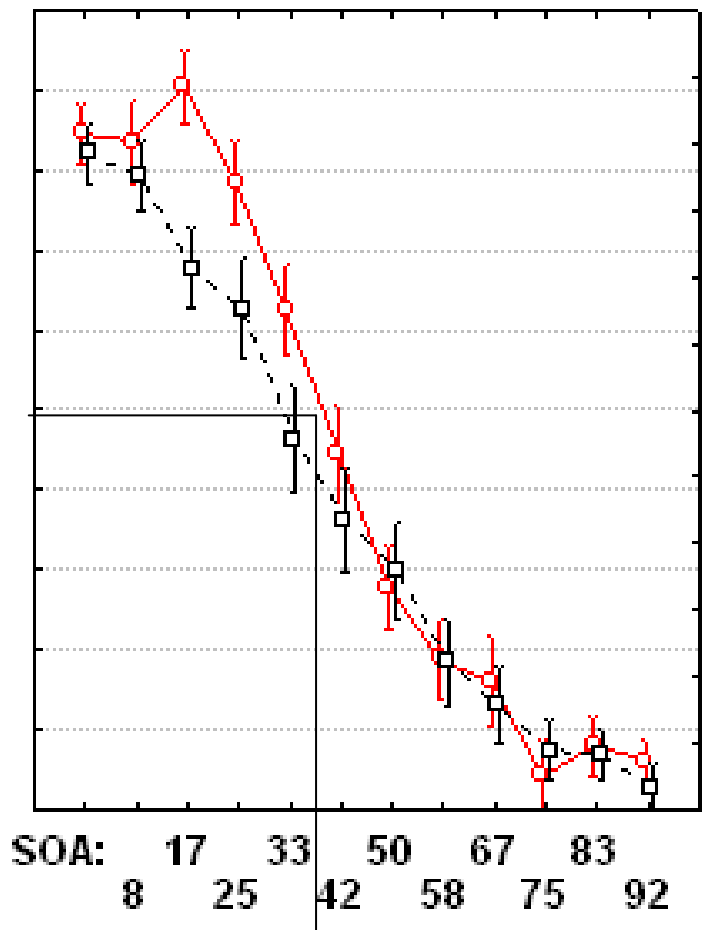
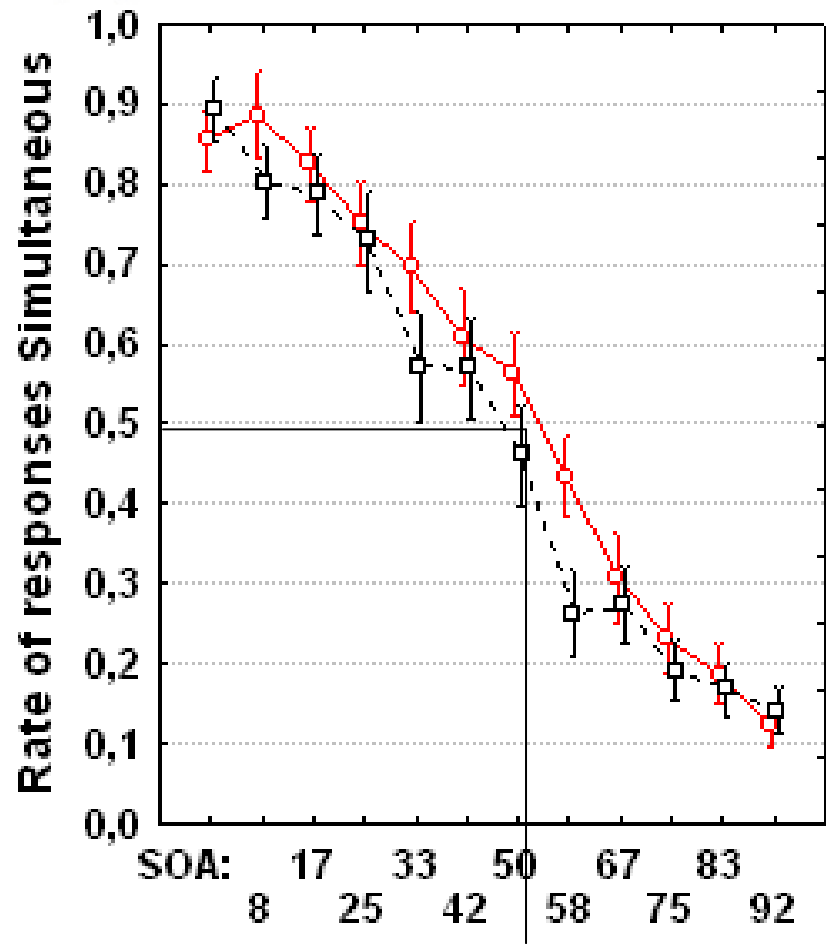


Simultaneous response

Asynchronous response



SQUARES on the LEFT
SQUARES on the RIGHT



PATIENTS

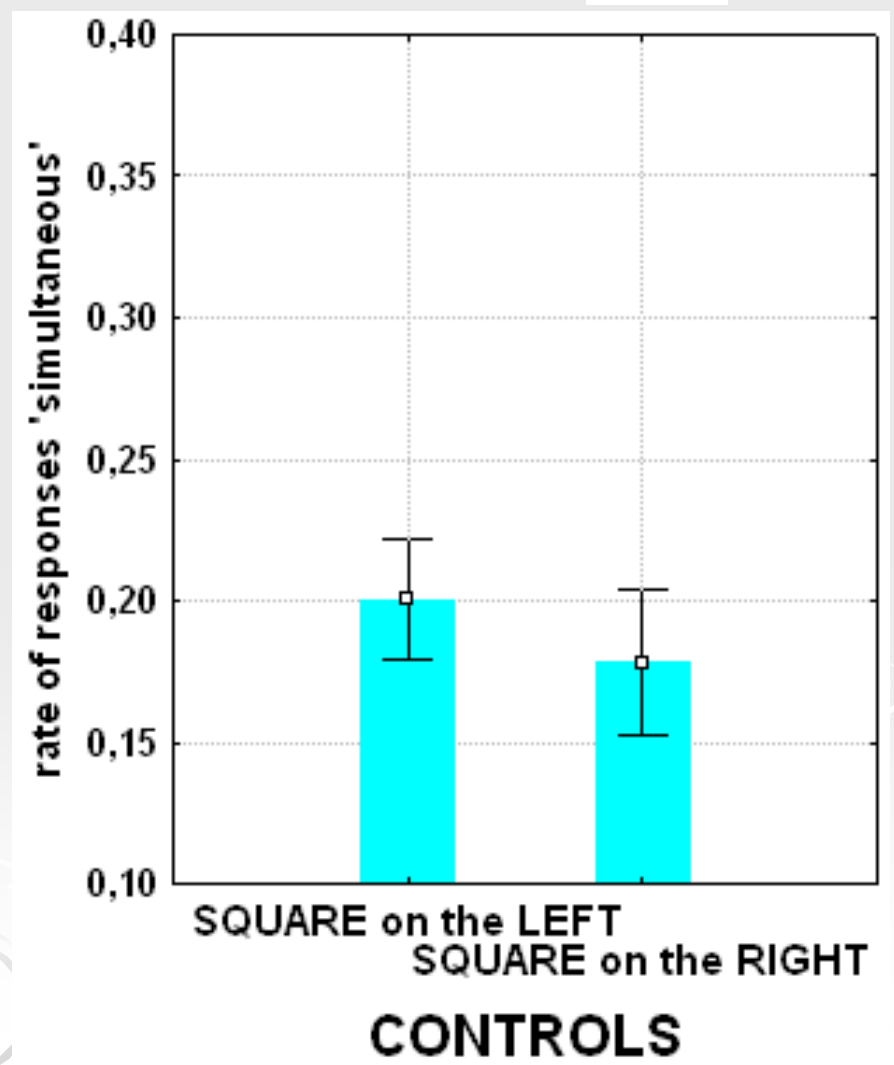
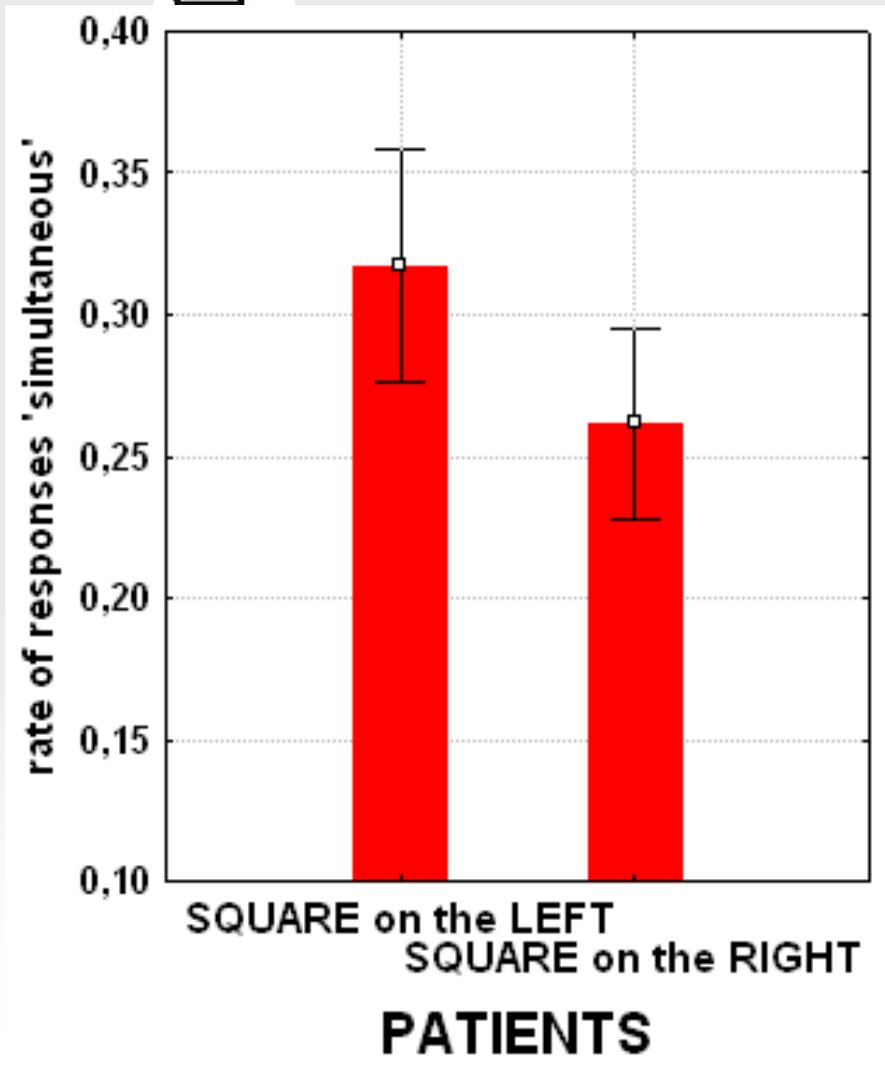
CONTROLS

***Simultaneous
response***



Above threshold

***Asynchronous
response***

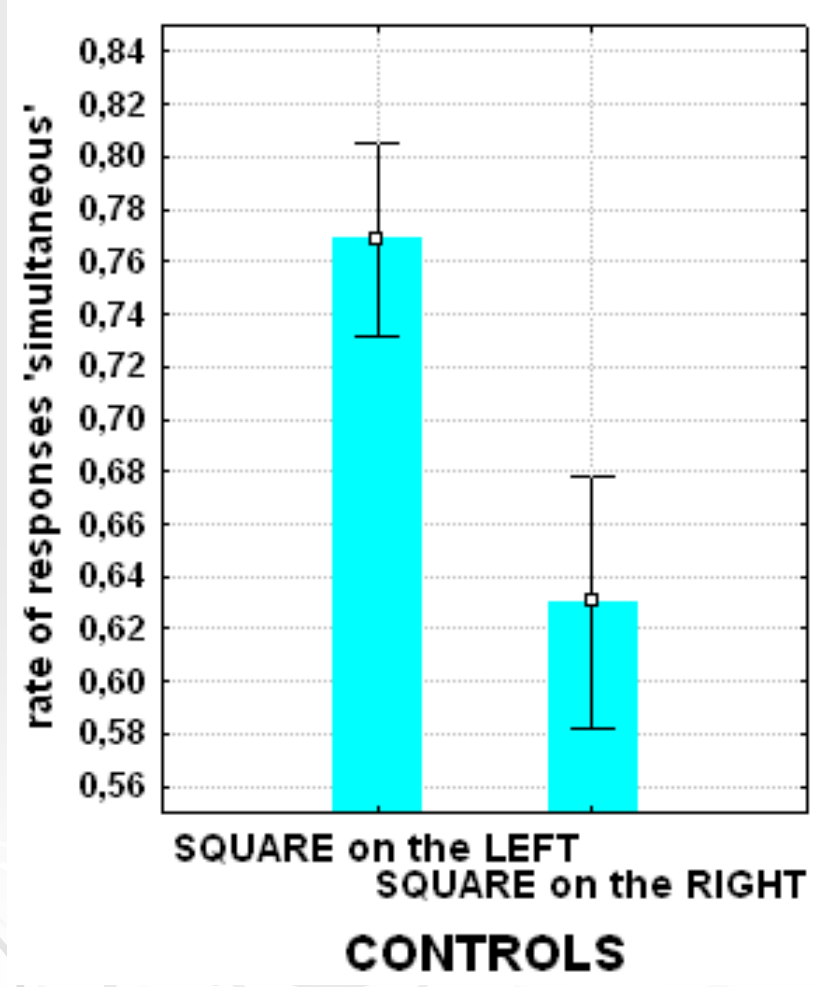
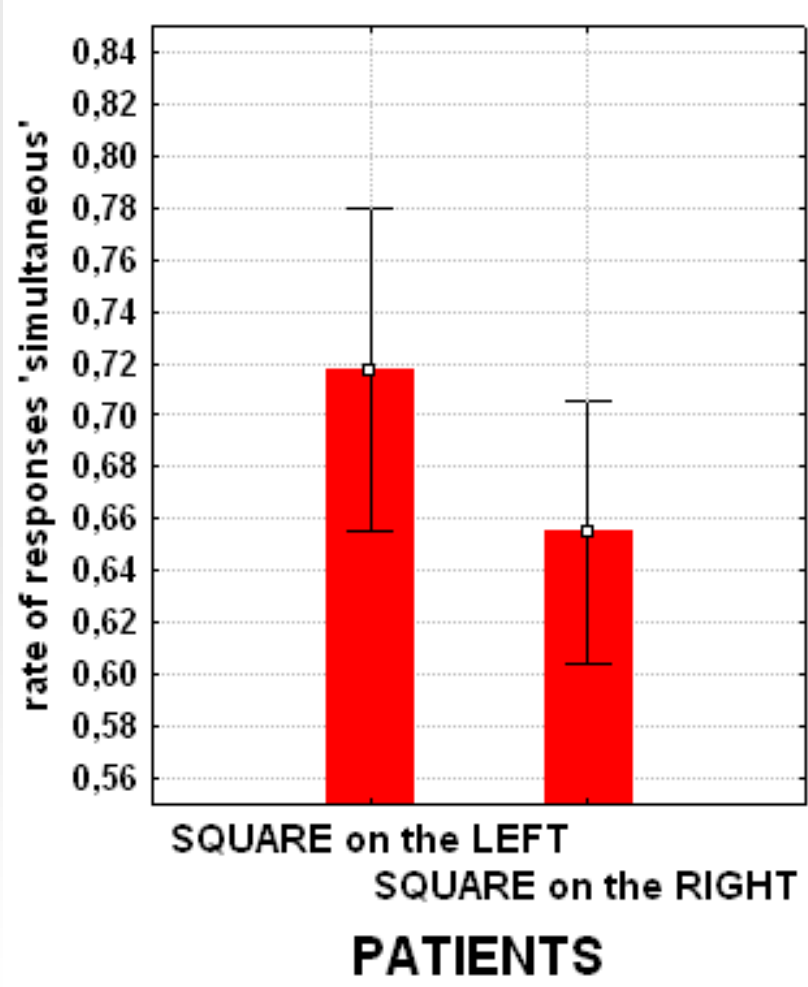


Simultaneous response

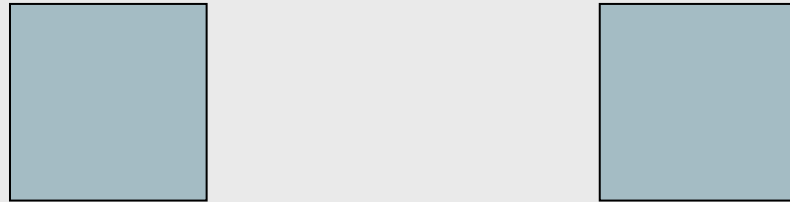


Below threshold

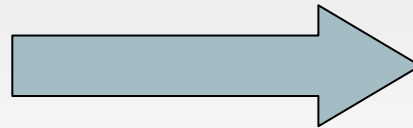
Asynchronous response



- The critical analysis regarded what happened when the two squares appeared in two different hemi-fields.



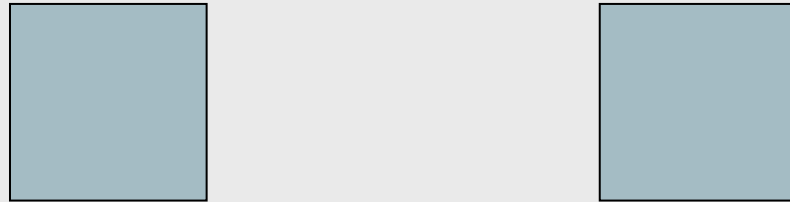
***Simultaneous
response***



***Asynchronous
response***



- The critical analysis regarded what happened when the two squares appeared in two different hemi-fields.



***Simultaneous
response***



***Asynchronous
response***



The question is

- Is the response biased by the 1st or the 2d square?

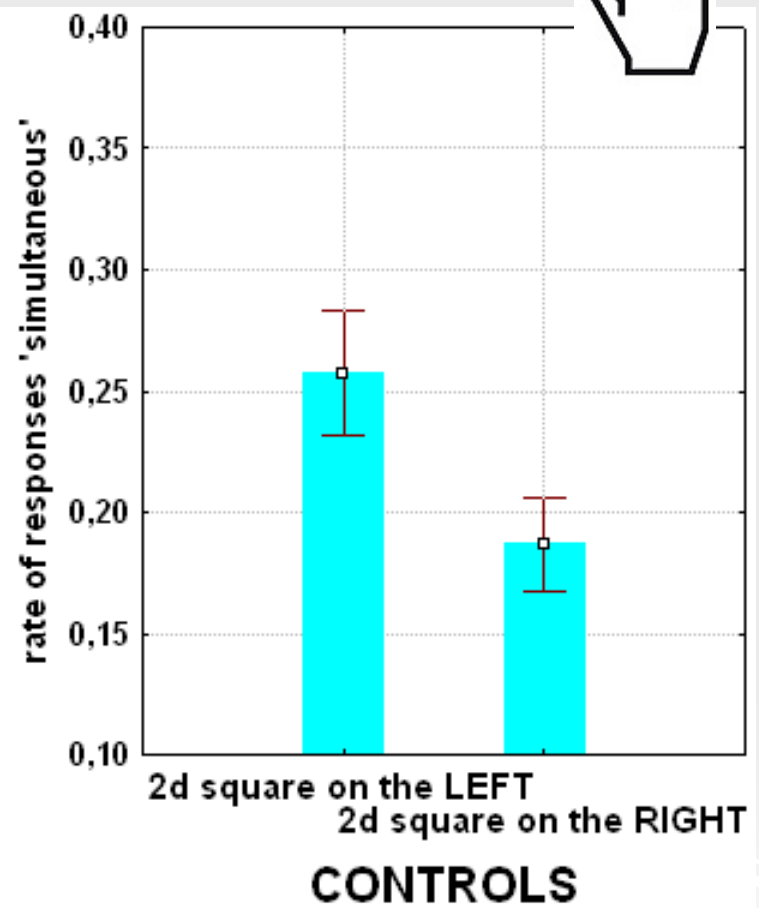
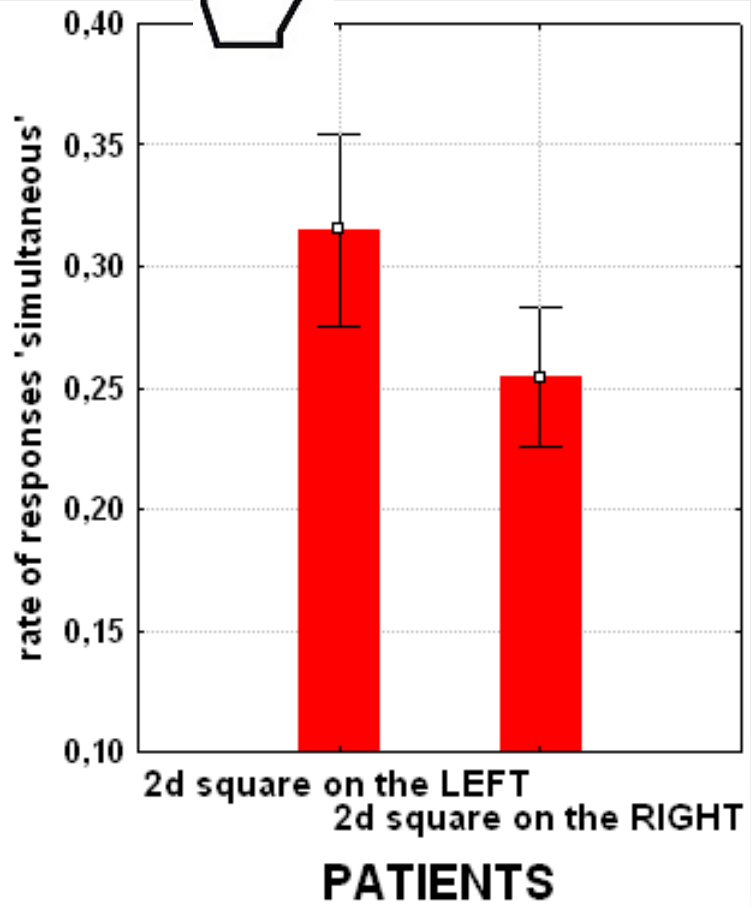


Simultaneous response



Above threshold

Asynchronous response

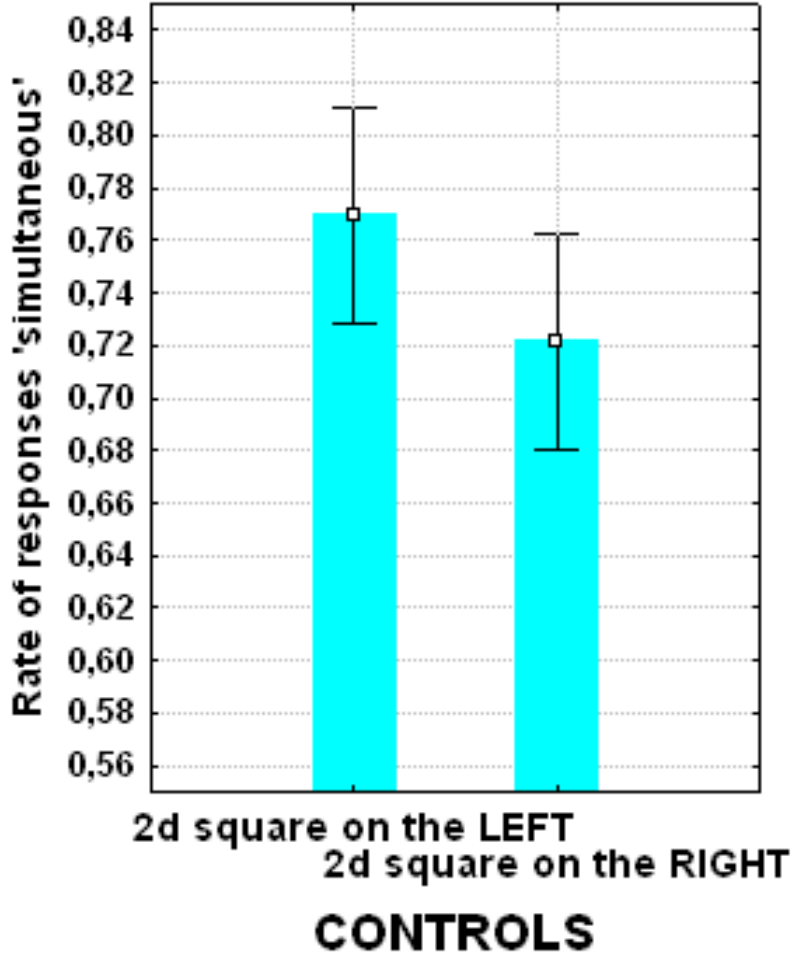
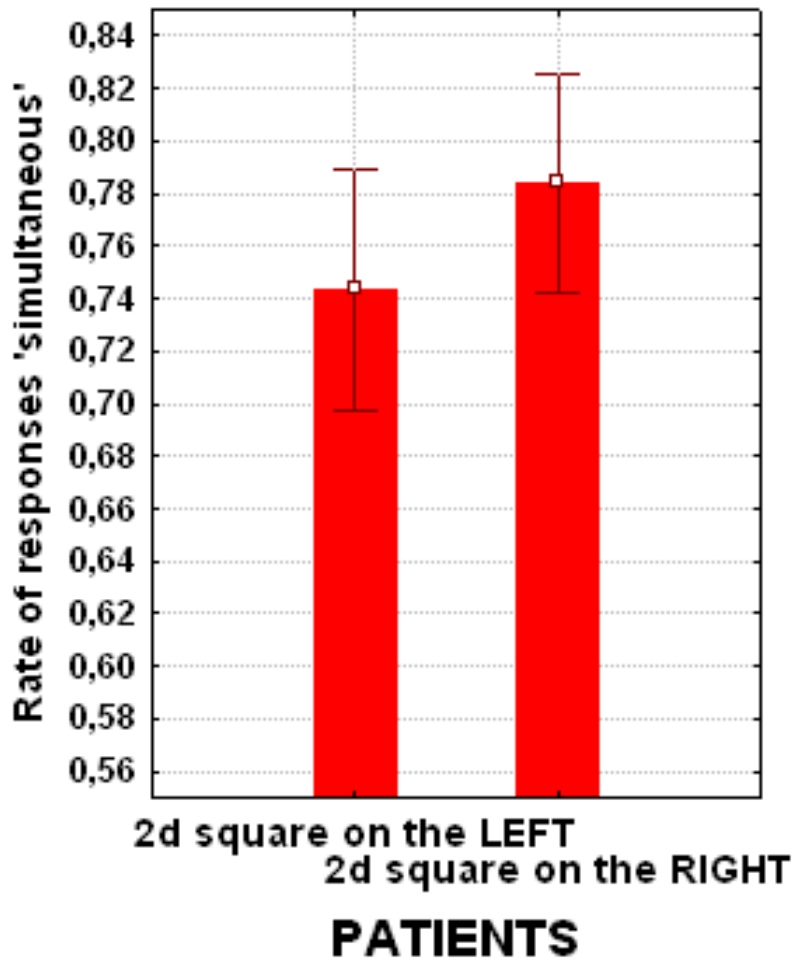


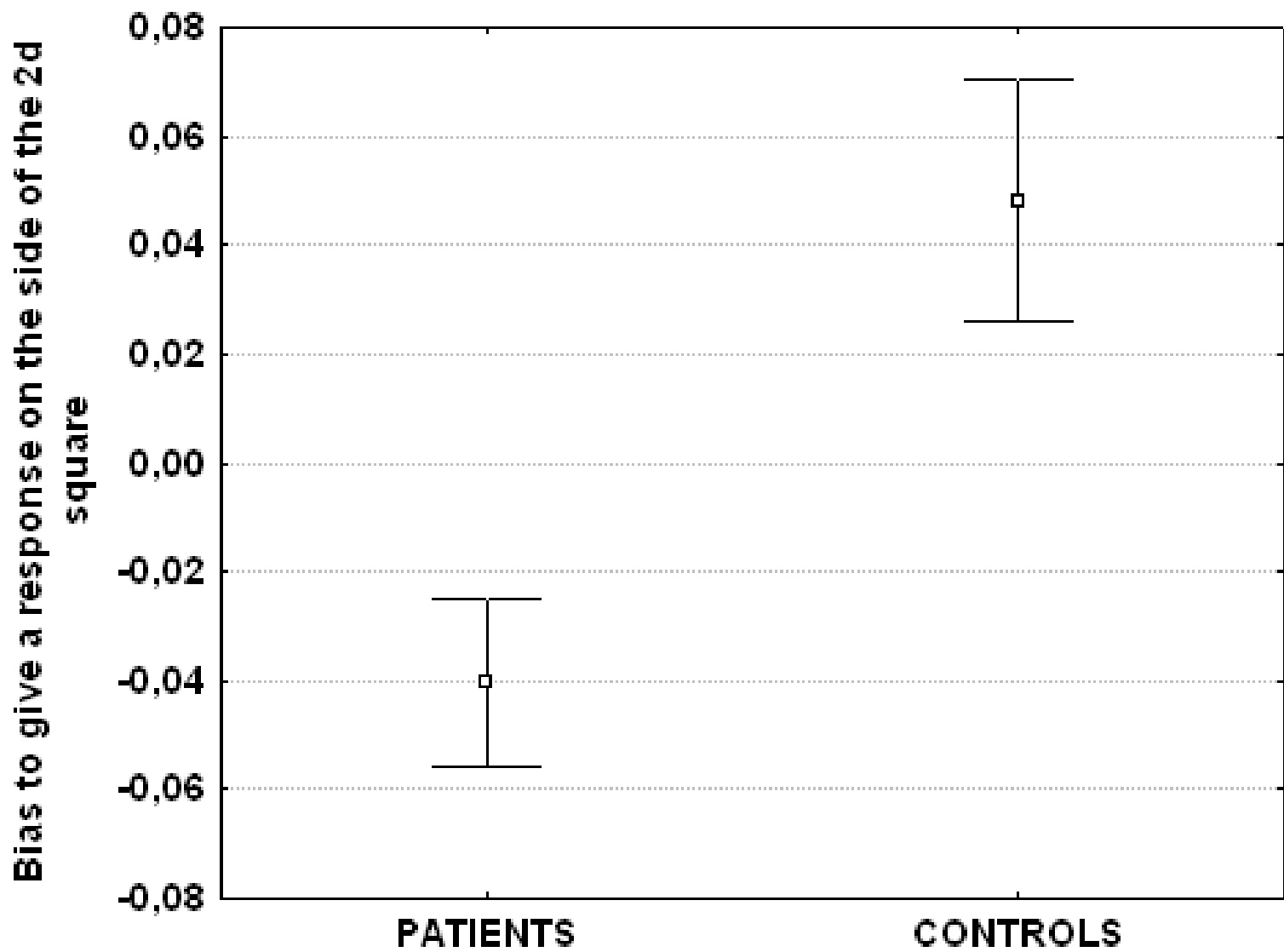
- All subjects do the task as instructed. The expectancy regarding the 2d square and a possible sense of direction lead to a Simon effect on the side of the 2d square.

Simultaneous response

Below threshold

Asynchronous response





Even below threshold

- There is enough information to distinguish between the 1st square and the 2d square
- Else, if the two squares were really perceived as synchronous at all levels of processing, there should be no Simon effect.



- A slight asynchrony does not lead to fusion of events as strict synchrony would.

In controls

- When there is no conscious perception of asynchrony, there is still some expectancy regarding the 2d stimulus.

In patients

- Expectancy appears to be disturbed in patients.

- It does not necessarily mean that the origin of the alteration is rooted in automatic processes.
- The lack of expectancy regarding the 2d stimulus might be due to several impairments in patients



- Expectancy is integral to the sense of time continuity. ‘Sub-threshold’ impairments might be related with the enlarged time window itself.



- Patients might be impaired at selecting the different locations of the stimulus in anticipation. It would be consistent with visual perception studies suggesting top-down impairments in patients (Giersch & Rhein, J Abn Psychol, 2008; Van Assche & Giersch, Schizophrenia Bull, 2009)



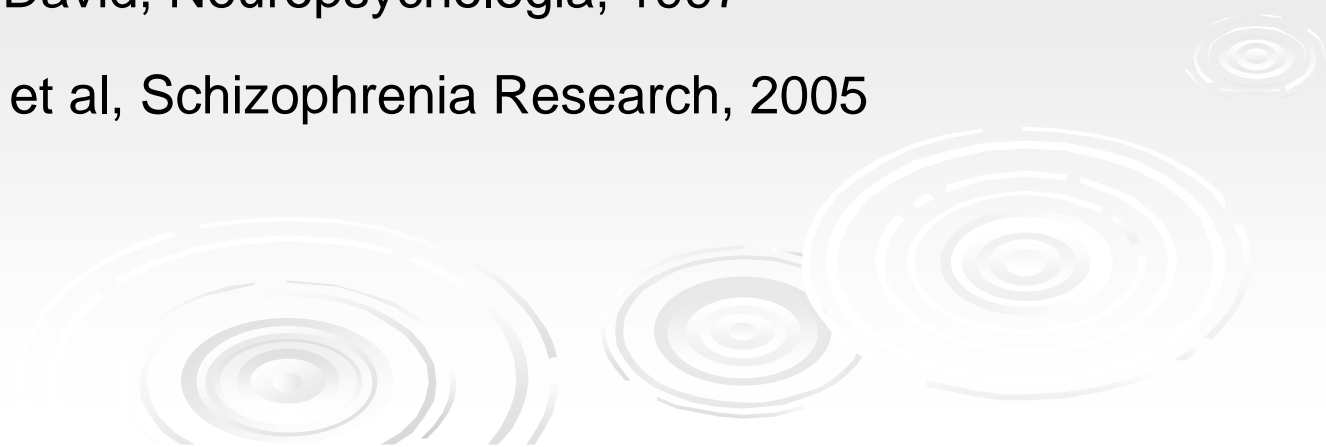
Visual organization impairments in patients



Patients are usually believed to be impaired at using global configurations: Desorganized in their perception like in their behaviour.

Phillips & David, *Neuropsychologia*, 1997

Minassian et al, *Schizophrenia Research*, 2005



However,

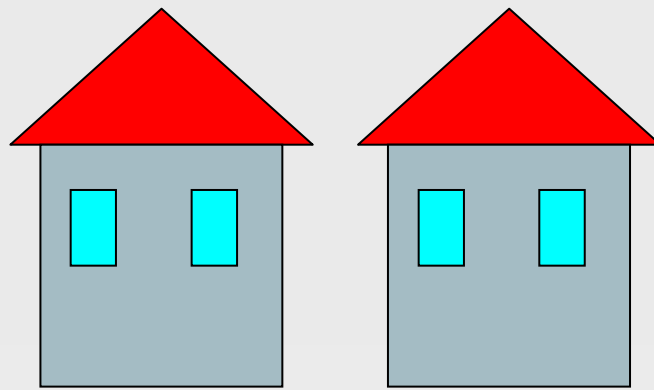
- The mechanisms of these impairments remain controversial. This makes it difficult to understand in which conditions patients will be disturbed.

(see Uhlhaas, Psychological Bulletin, 2005, for a review):

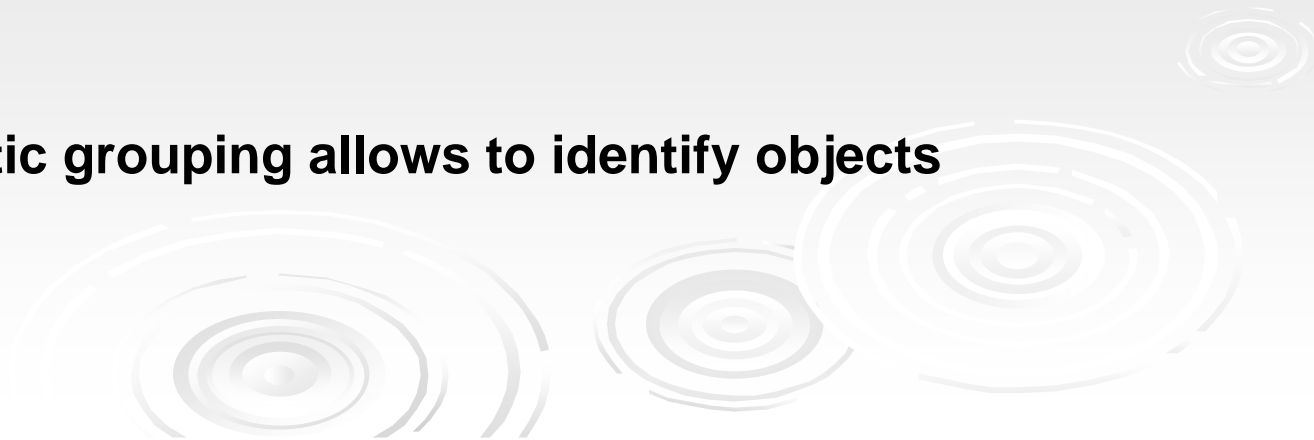
- Visual perception involves different ways of 'organizing' information.

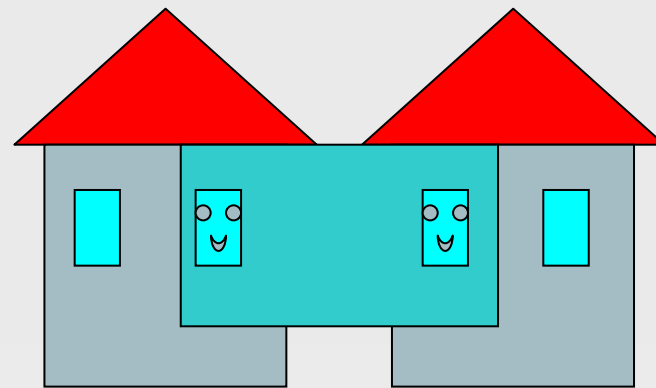
Low-level and automatic grouping? Like grouping by proximity or connectors.

Top-down control on grouping?



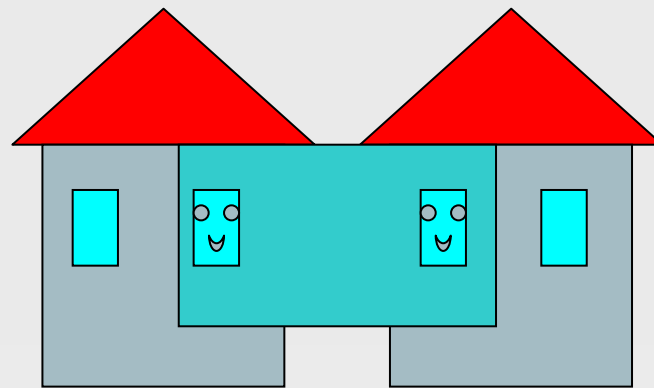
Automatic grouping allows to identify objects



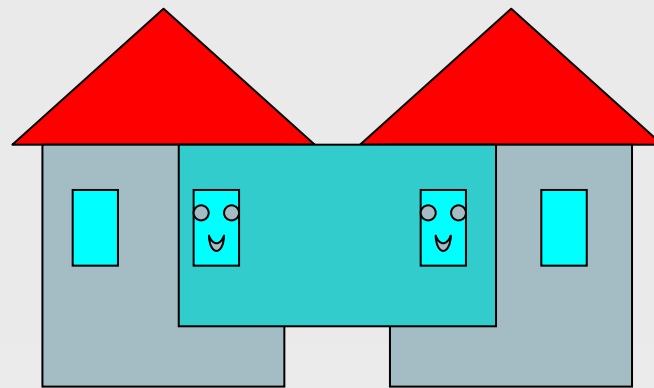


But it is possible to mentally re-group information in a different way

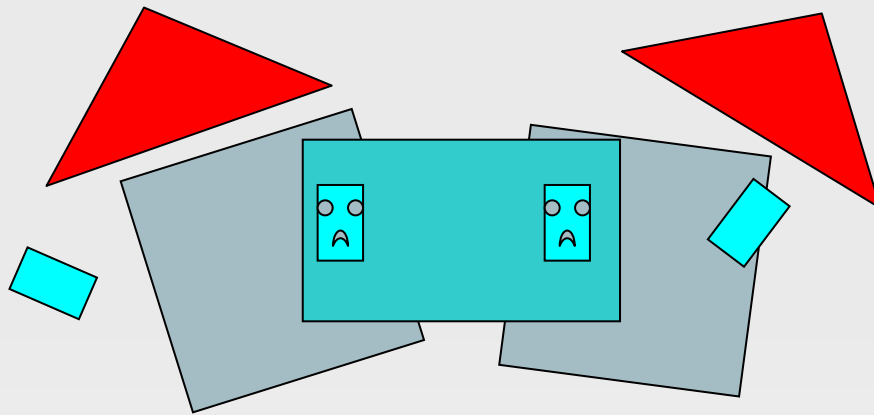




This is not trivial: regrouping the two windows means separating them from other items (the other windows, the roof...)

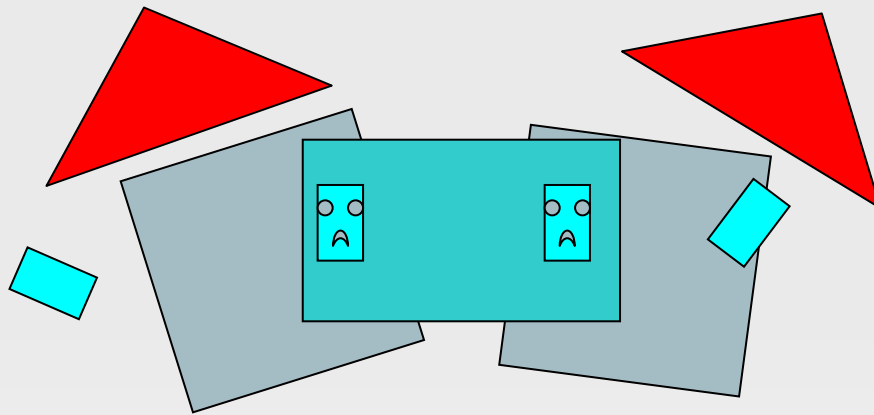


Separating the different items composing the houses entails the risk of fragmenting the house

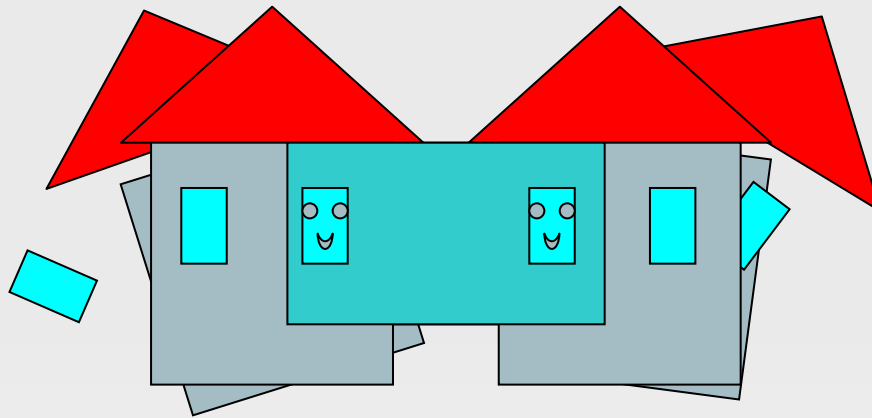


Separating the different items composing the houses entails the risk of fragmenting the house

Parallel pathways have been described, that subserve the processing of local and global processing. However, in our example, global information is the two houses, and local information is one window. The pair of windows is neither local nor global

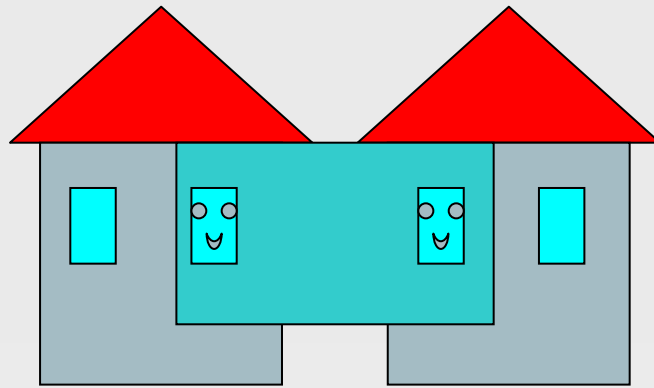


Top-down control is required to re-organize information without inducing a fragmentation of information.



Top-down control is required to re-organize information without inducing a fragmentation of information.

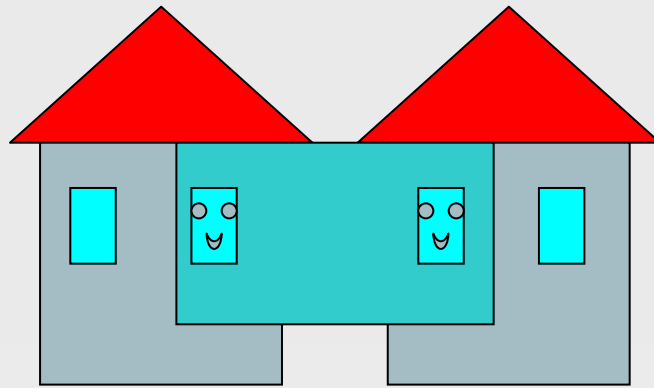
We argue this relies on the building of a representation unifying the two windows.



Top-down control is required to re-organize information without inducing a fragmentation of information.

We argue this relies on the building of a representation unifying the two windows.

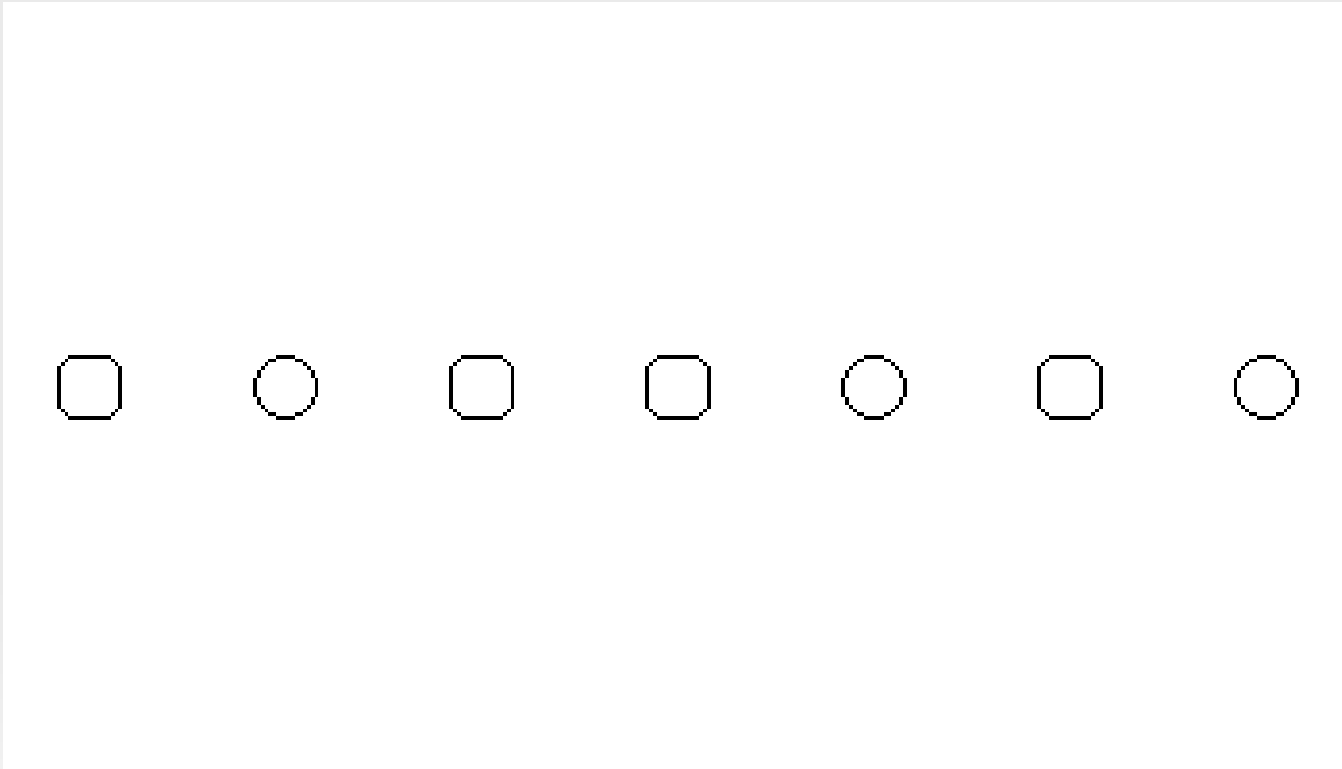
This would be impaired in patients with schizophrenia.



Repetition Discrimination Task (Beck & Palmer, 2002)



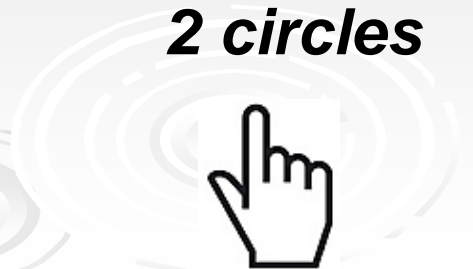
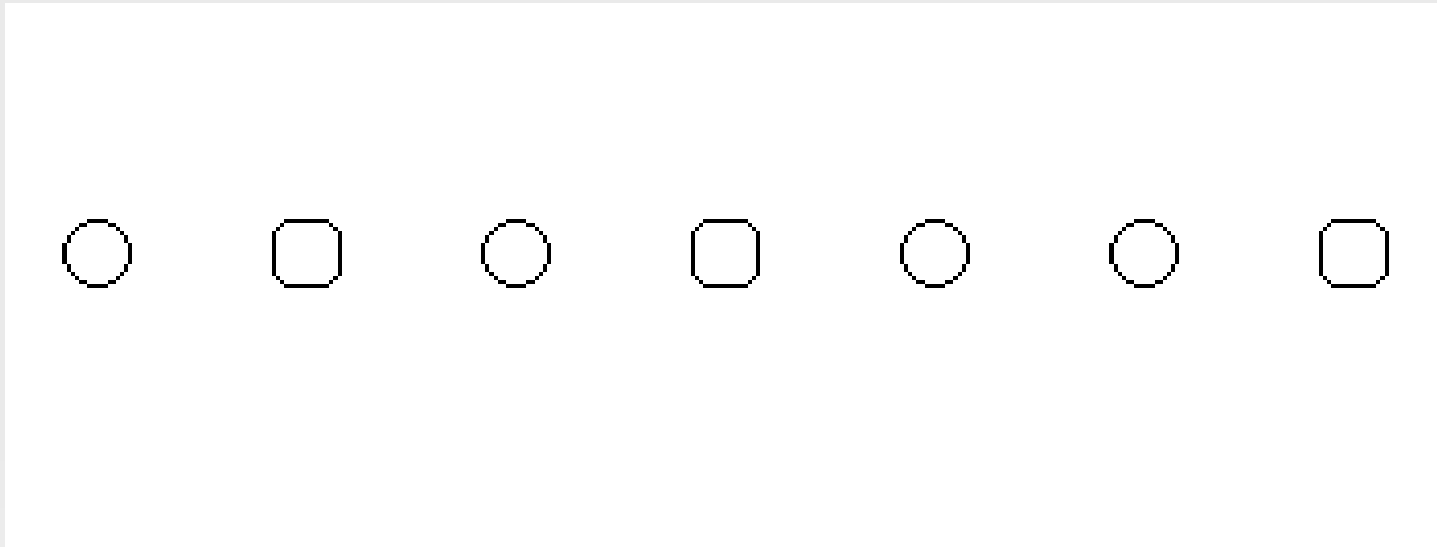
Circles and squares are displayed in alternance. Two adjacent figures are identical. 2 squares or 2 circles?



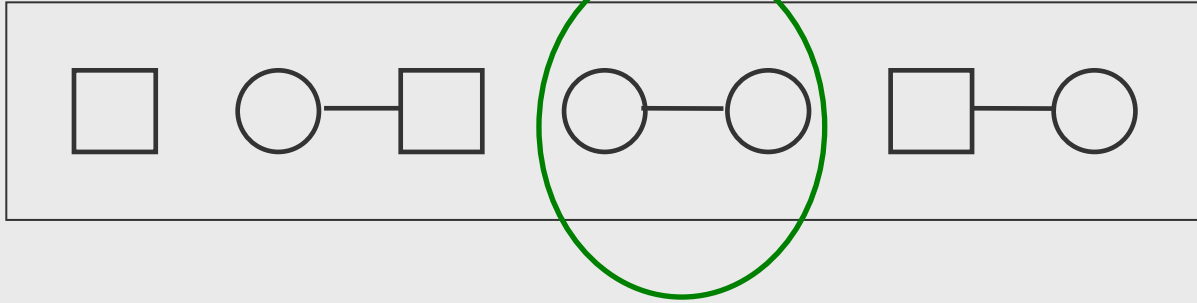
2 squares



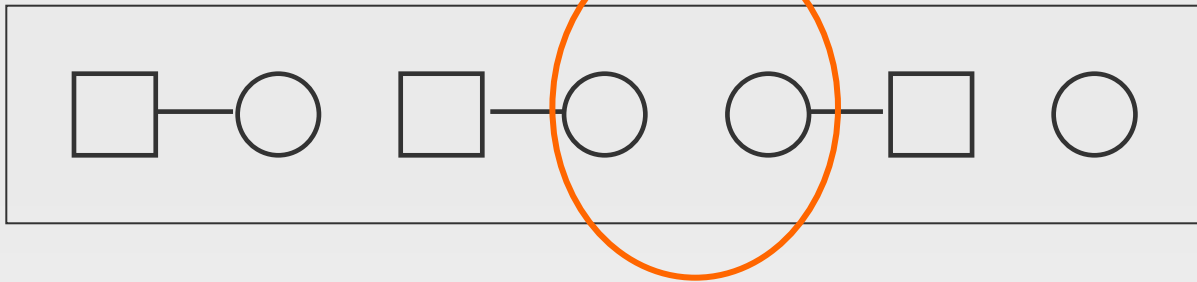
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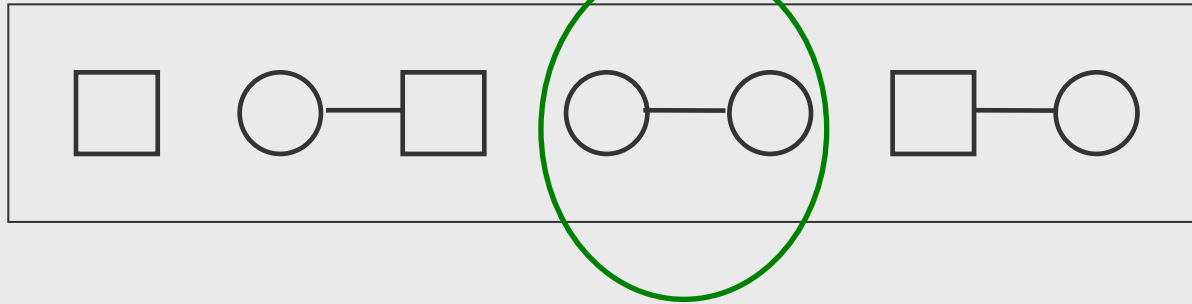
Within-group



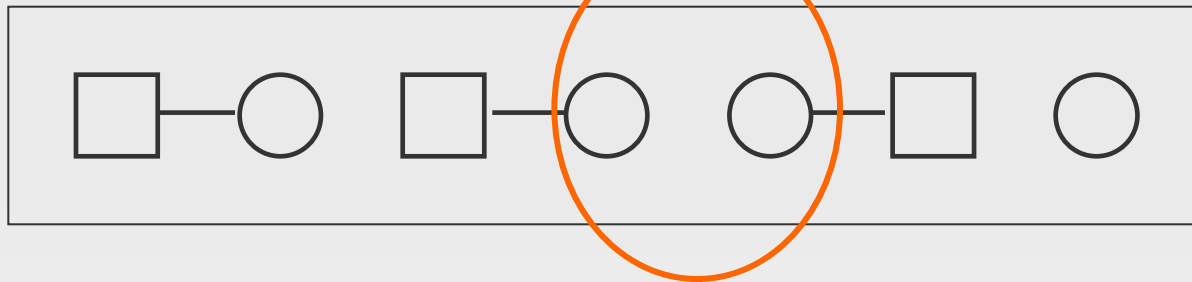
Between-group



Within-group

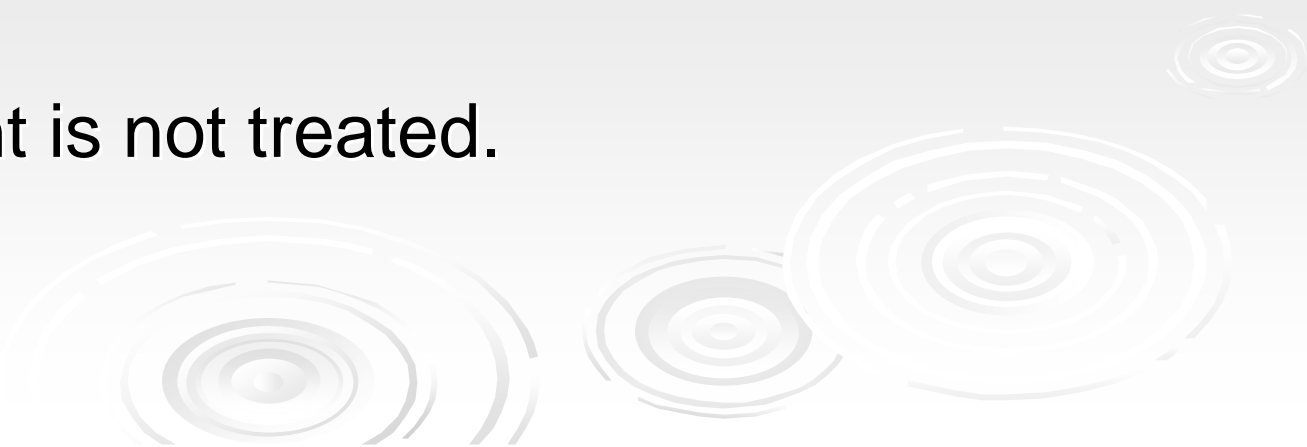


Between-group

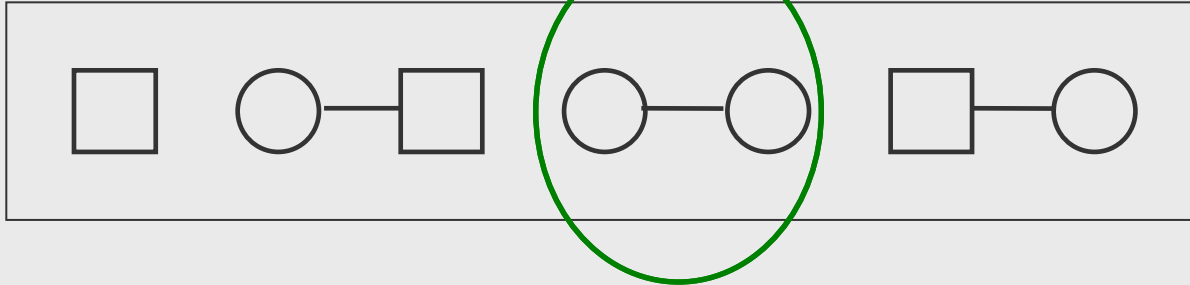


RTs for within-group trials are faster than for between-group trials : shows the benefit provided by grouping.

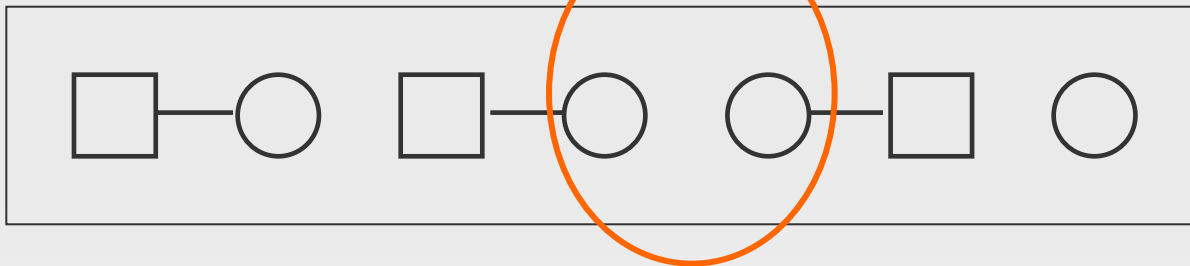
23 stabilized patients vs 23 matched controls

- AGE Patients: 35 – Controls: 35 years
 - Education level: 11.6 in patients vs 11.7 years in controls
 - Patients are treated with atypical neuroleptics: Chlorpromazine equiv. 296
 - PANSS = 77.5 (positive 17.8; negative 20.4; global 39.7)
 - One patient is not treated.
- 

Within-group



Between-group



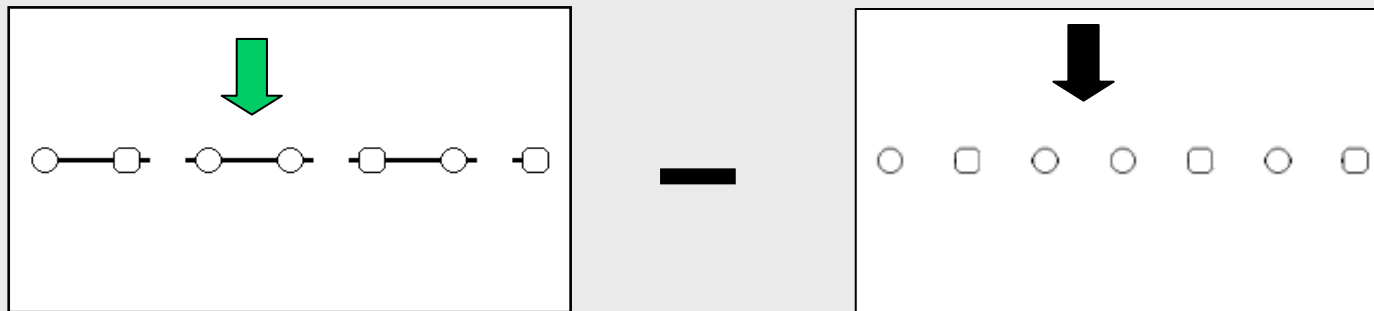
In this precise configuration, the difference between within-group and between-group trials was lower in patients with schizophrenia than in controls.

But due to between-group trials.

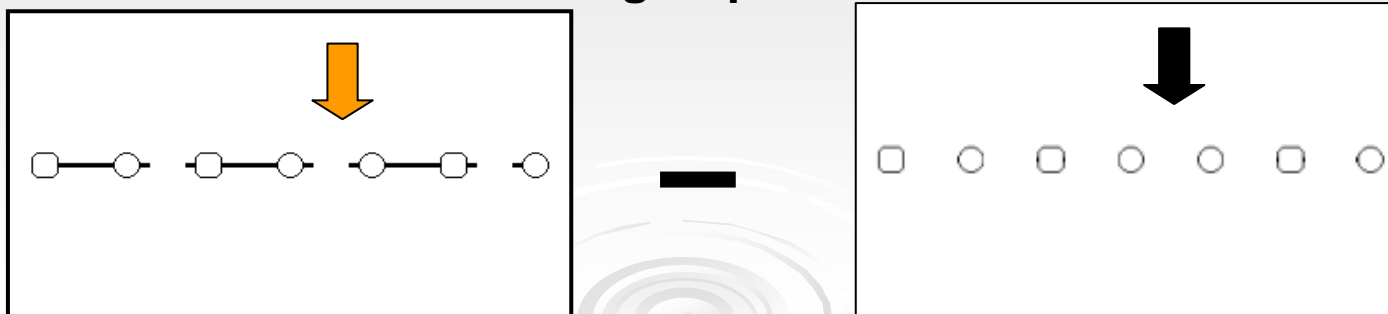
The results show that organizing information takes time:
RTs are longer when there are connectors than when they are absent (i.e. in baseline).

We compared RTs when connectors were present vs. when they were absent:

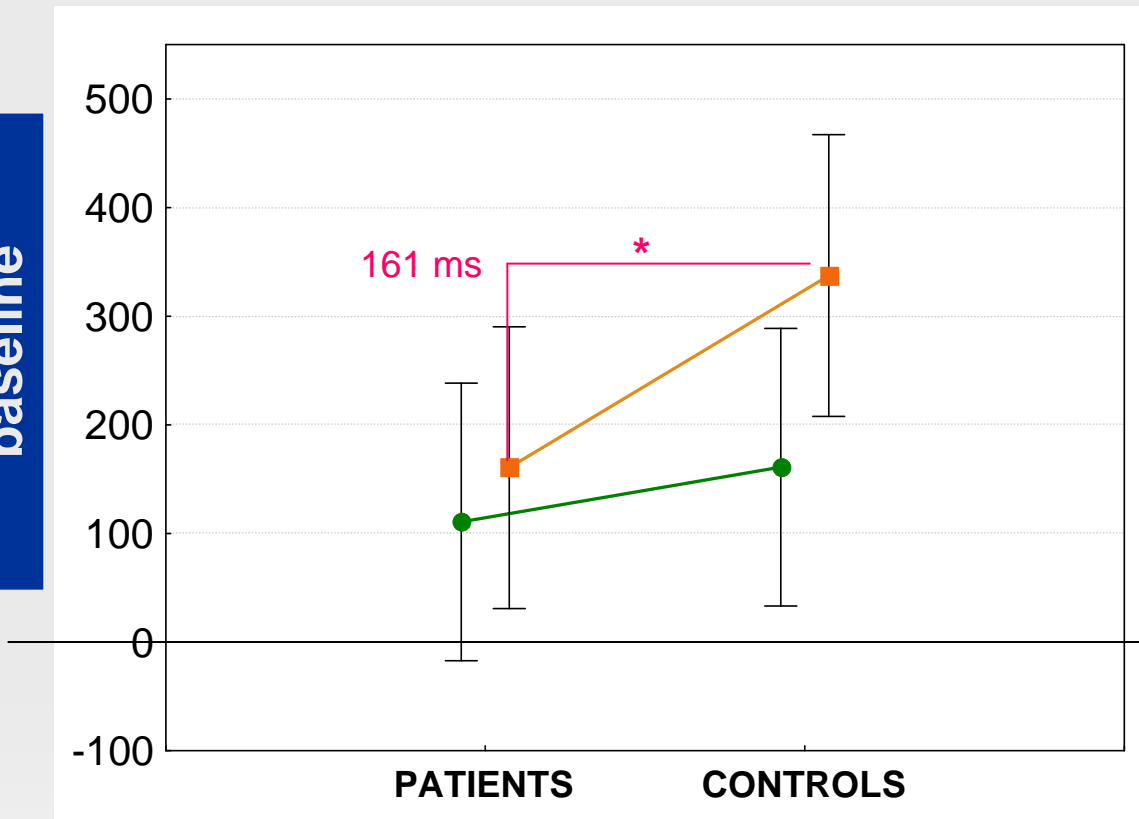
Within-group - baseline



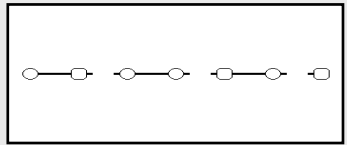
Between-group - baseline



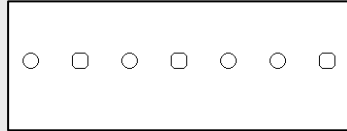
**RT connecteurs -
baseline**



Connectors



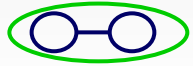
Baseline



Baseline level

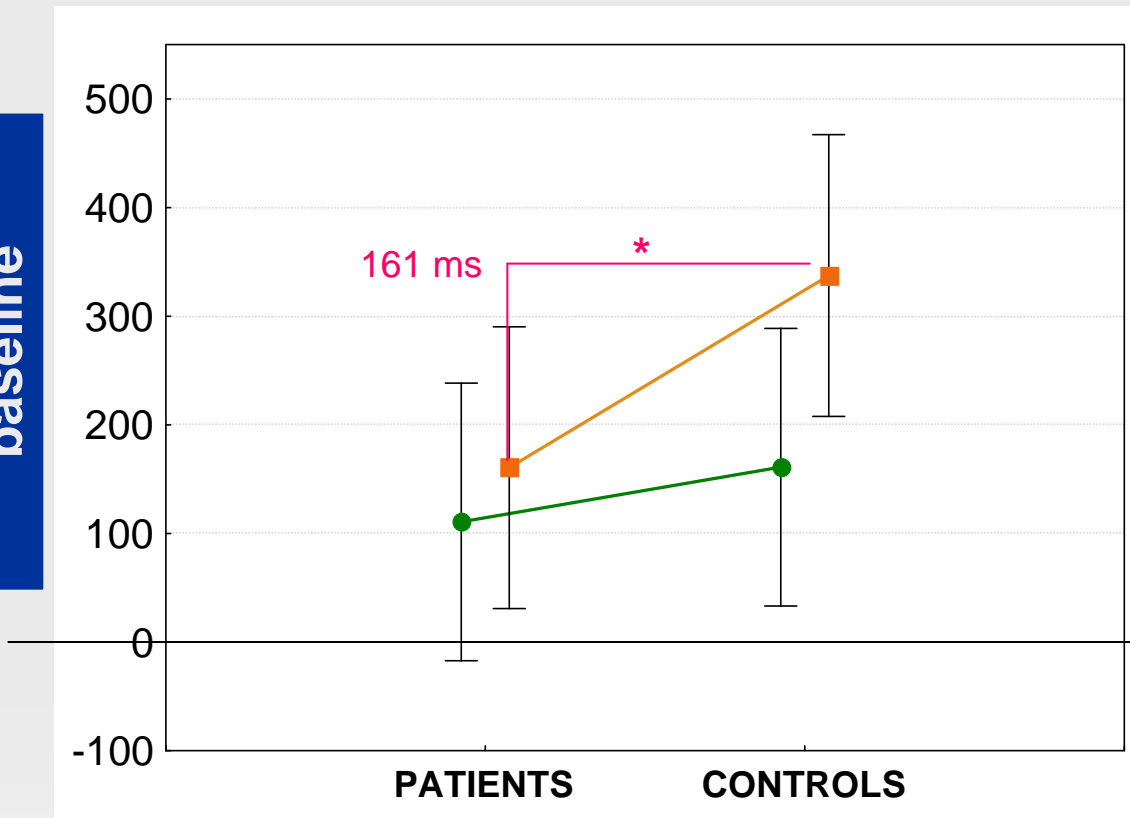


Between-group

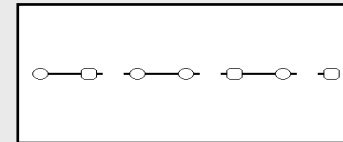


Within-group

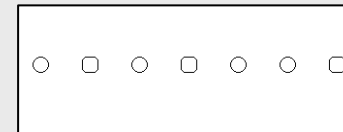
**RT connecteurs -
baseline**



Connectors



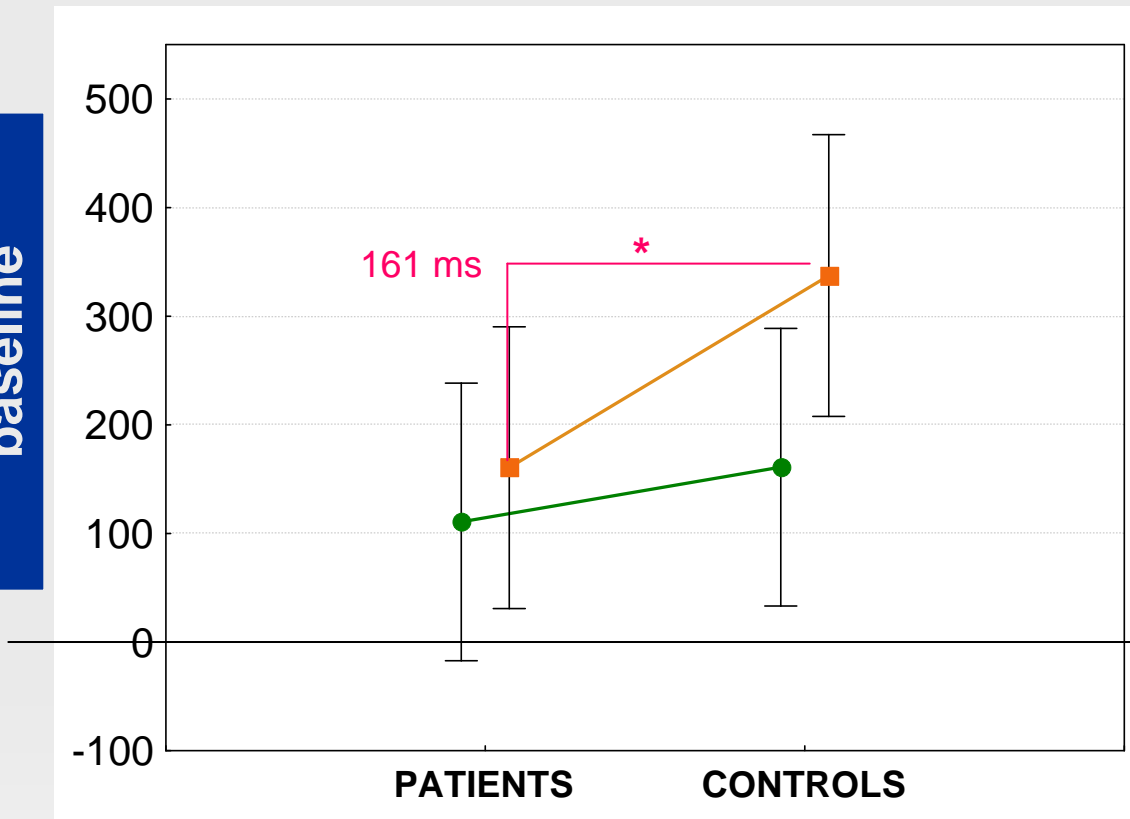
Baseline



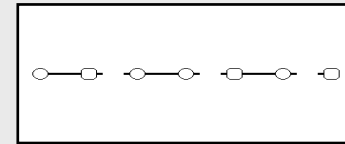
RTs increase in controls for between-group trials, relative to baseline, because selecting between-group pairs requires time



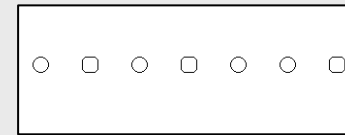
**RT connecteurs -
baseline**



Connectors



Baseline



**Patients process
between-group
pairs like baseline.**

 **Between-group**

 **Within-group**

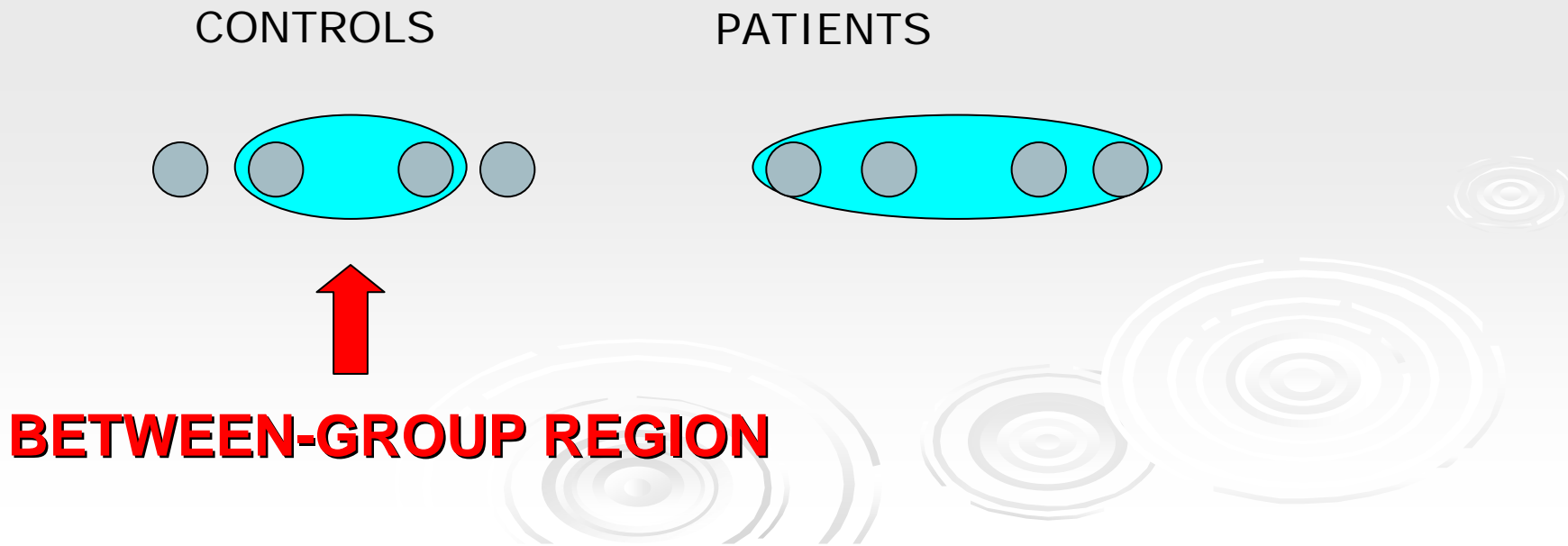
Patients have a difficulty to select
between-group regions



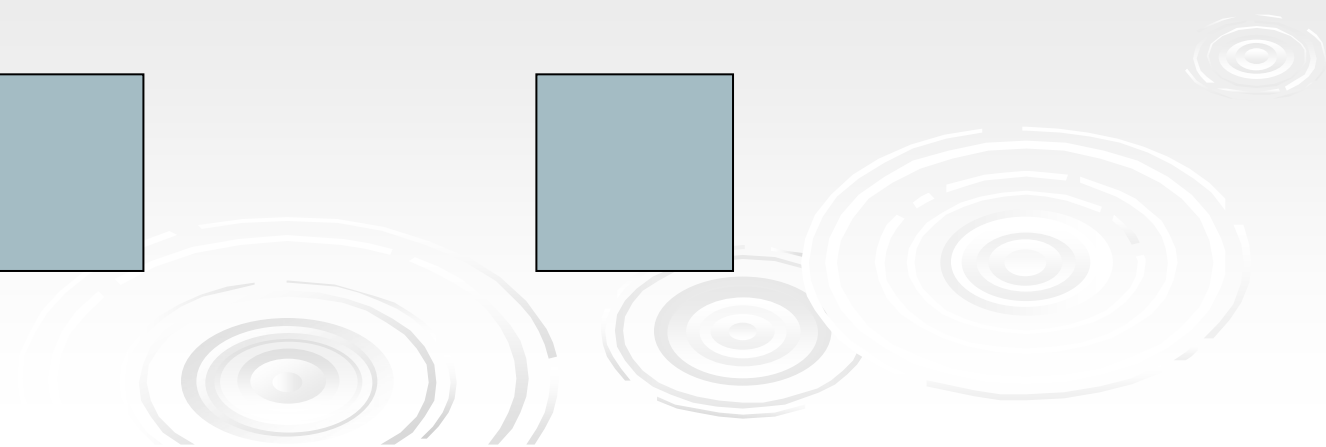
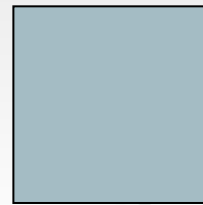
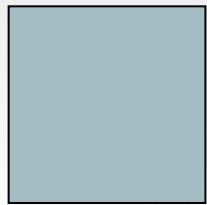
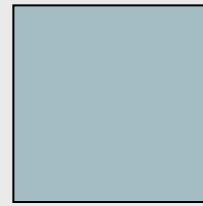
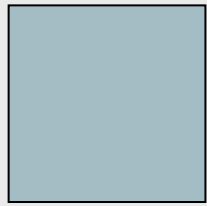
Patients have a difficulty to select between-group regions

Eye-tracking shows that healthy controls are able to prioritize a pair of objects even if each object belongs to a different group.

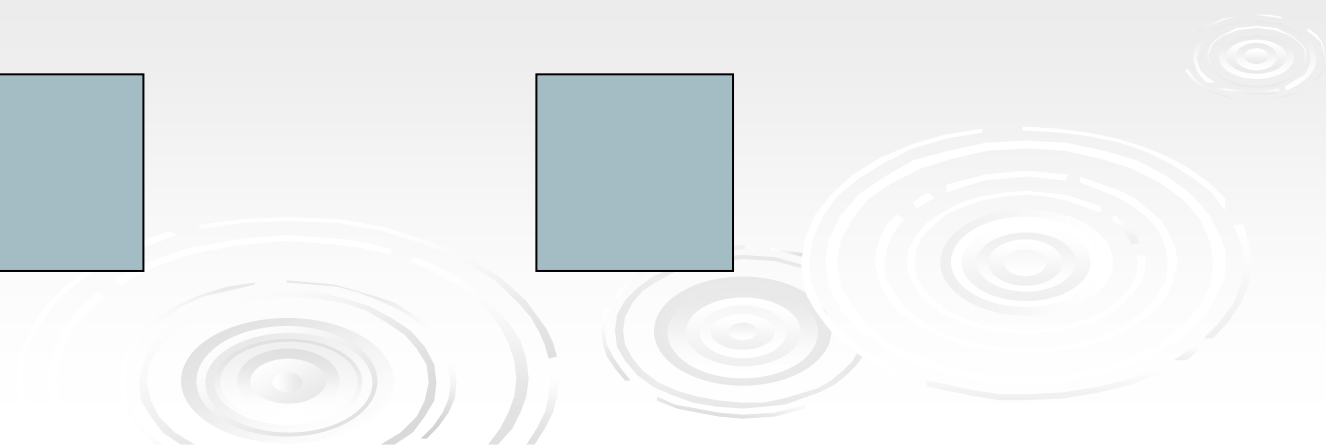
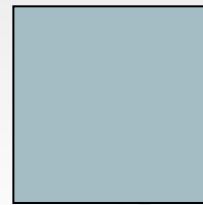
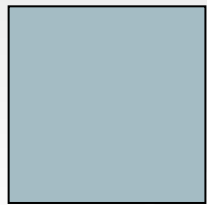
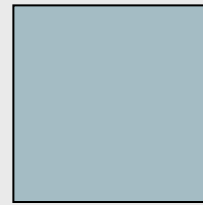
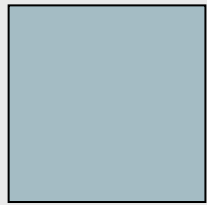
Patients are not able to do so selectively.



What does this mean for the
simultaneity/asynchrony
detection paradigm?



Do the patients have a difficulty to compare the onsets of two squares because they cannot select them together?



Results yet to come....



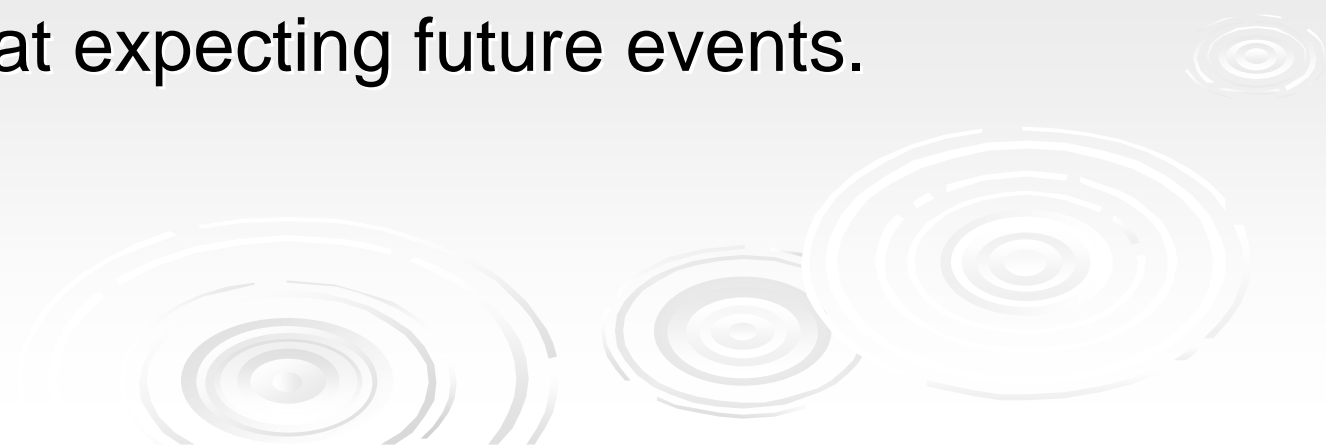
- Whatever the origin of the ‘expectancy’ impairment, this might have important consequences for patients.



In sum,

Sub-threshold perception of asynchrony is observed in controls, but appears to be qualitatively distorted in patients. Maybe even when stimuli are part of the same group?

It might mean that patients have a fundamental impairment at expecting future events.



In sum,

Impaired expectancy in patients might be due to disturbed attentional top-down control or to the enlarged time window itself.

We expect this question to be soon resolved???

Next question will then regard the implication of this impairment, concerning visual organization but also other cognitive functions.

The aim here is to get a more complete picture of how cognitive impairments interact and lead to clinical symptoms in patients.

Acknowledgements

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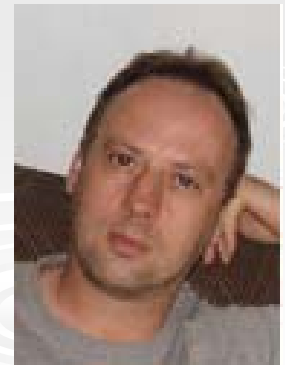
Janina Seubert



Jack Foucher



Weixin Wang



Mark Elliott