Effect of Gaze Direction on Orienting of Attention in Patients with Schizophrenia: Attention or Social Cognition Deficit?

Maria Chiara Pino[1]*, Melania Mariano[2], Alessandro Valchera[3], Marco Valenti[2,4], Domenico De Berardis[5,6] and Monica Mazza[2]

[1]Department of Life, Health and Environmental Sciences, University of L'Aquila, L'Aquila, 67100, Italy
[2]Department of Applied Clinical Sciences and Biotechnology, University of L'Aquila, L'Aquila, 67100, Italy
[3]Hermanas Hospitalarias, FoRiPsi, Villa S. Giuseppe Hospital, Ascoli Piceno, 63100, Italy
[4]Reference Regional Centre for Autism, Abruzzo Region Health System, L'Aquila, 67100, Italy
[5]NHS, Department of Mental Health, Psychiatric Service of Diagnosis and Treatment, Hospital "G. Mazzini", ASL 4, Teramo, 64100, Italy
[6]Department of Neurosciences and Imaging, Chair of Psychiatry, University "G. D'Annunzio" of Chieti, Chieti Scalo, 66100, Italy

Abstract

Introduction: the ability to use the gaze direction of another person to guide attention is part of a complex construct named Social Cognition. Schizophrenics showed impairments in domains of social cognition.

Aim and objectives: the aim of this study was to investigate whether gaze cueing of attention is compromised in schizophrenic subjects.

Materials and methods: we tested 18 schizophrenics and 18 controls who were presented with gaze and arrow cues in a modified version of the Posner's spatial cueing paradigm.

Results: The performance of schizophrenics was compromised when the cue is represented by the gaze rather than by the arrow. In fact, our results showed that two groups differ only for gaze condition both in reaction times ($F_{1,34}$=61.557; p=0.0001) and number of errors ($F_{1,34}$=6.39; p=0.002). Moreover, the correlation analysis showed that the Eyes Task negatively correlates with invalid condition when the cue was the gaze (r=-0.504, p=0.03). This result underlines the crucial relation between the emotional recognition capacity of the another person's gaze and the orienting of attention capacity through the interpretation of other people's gazes. These capacities seem to be precursors for good development of Social Cognition.

Conclusion: Taken together, these findings suggest that schizophrenics showed a specific deficit in social attention, that is part of social cognition construct. Deficit in attention to gaze direction in patients with schizophrenia may contribute to interpersonal and social cognitive difficulties. Thus, the gaze interpretation ability can be considered as an important part in rehabilitation strategies for schizophrenics.

Keywords: Attention; Cues; Gaze; Schizophrenia; Social cognition

Introduction

Schizophrenia is a complex and widespread disorder, that can be disabling due to a multiplicity of socio-cognitive deficits. Social cognition refers to a relatively large number of psychological constructs that range from complex concepts, such as theory of mind (ToM), to more elementary concepts, such as emotion perception (EP), processing of social cues or social perception (SP), and empathic ability [1,2]. Social isolation and poor interpersonal skills mark the lives of many people with schizophrenia. This impairment may stem in part from deficits in interpreting the meaning of social cues and drawing inferences about other people's thoughts, intentions, and feelings [3-5] and these impairments significantly compromise their social functioning [6]. Several studies showed that social cognition ability consists of a range of precursor skills, including following eye-gaze, establishing joint attention, imitation, pretend play, and emotion recognition [7,8]. One of its most intriguing symptoms in schizophrenia is an abnormal sensitivity to gaze [9]. The ability to detect the direction of another person's gaze and to shift our own attention reflexively in the same direction facilitates the sharing of attention with other people [10]. In humans, the direction of someone's gaze provides insight into that person's focus of interest and state of mind, and there is increasing evidence linking abnormal gaze behaviours to clinical conditions such as schizophrenia and autism [11]. Adolphs [12] has proposed a model that describes three steps of a correct development of social cognition: (1) "social perception" which is the detection of social stimuli; (2) "central social cognition," which entails the recognition, evaluation, and interpretation of material; (3) "social behaviour," which is the effecting of the individual's response [13].

The social stimuli are powerful signals but are often processed implicitly, outside the focus of attention. Several studies have shown that individuals with schizophrenia have difficulty interpreting social and emotional cues such as gaze direction [5,14]. One's gaze allows a person to perform several important social functions that range from the regulation of conversations with others to managing of a social position. Gaze perception activates a network of brain regions, including both the posterior superior temporal sulcus (pSTS) and the amygdala, which are central to the perception of biological motion and social cognition [7,15]. Direct gaze also improves cognitive functions such as recognition memory for faces, categorization of facial gender and selected facial expressions [16,17].

For this reason, it has been suggested that orienting of attention can be a precursor for good ToM development [18]. Several studies showed that as early as 2 to 3 months, new-born babies look preferentially at the eyes of a face rather other things, [19] and after 3 months they are also able to discriminate changes in an adult's gaze direction.

In particular, observing people's orienting-of-attention ability to social cues, such as gaze, allows us to understand important information. The study of this capacity was pioneered by Posner in the 1980s [20]. In his paper, Posner [20] used a simple model task in which subjects were asked to commit attention to a position in visual space other than a point of fixation. According to Posner's hypothesis, the orienting of attention is facilitated by a cue that indicates the exact position of the target. On the other hand, if the target appears in a different position from the cue, the attention must first be unlocked from the area indicated by the cue and then redirected to the new location. The high number of cognitive operations required to process an invalid target involves a great reaction time [21,22].

The aim of this study was to investigate whether gaze cueing of attention is compromised in schizophrenic individuals. For this reason, our study used a Posner paradigm to examine how gaze-direction and arrow cues guide attention in schizophrenia and matched controls. To our knowledge only a few studies have been carried out on schizophrenics with the purpose of studying the impact of gaze cue compared to non social signals on attentional orienting.

Methods

Participants

The study included 36 participants, 18 subjects (14 men and 4 women, mean age ± SD: 37.05 ± 9.20 years) affected by schizophrenia and 18 healthy subjects (14 men and 4 women; mean age=32.87 ± 4.91) to match age and education. The schizophrenic subjects were recruited from Hermanas Hospitalarias, FoRiPsi, Villa S. Giuseppe Hospital, Ascoli Piceno.

Diagnoses of these patients were made by a trained interviewer who used DSM-IV-R Structured Clinical Interview (APA, 2000). The participants' socio-demographic details are reported in Table 1.

At the time of testing, patients were taking antipsychotics whose mean chlorpromazine-equivalent dose [23,24] was 654.83 mg (SD 513.2). Participants' intelligence level was examined with Raven progressive matrices [25]. Written informed consent was obtained from all subjects before their participation.

Clinical assessment

The Italian version of the Brief Psychiatric Rating Scale-24 [26] (BPRS-24) was used. Each symptom on the 24-item scale was rated on levels rating from 1 to 7 (1¼ absence of symptoms; 7¼ very severe symptoms). The key score was composed of the amount of the complete scale. The following 5-symptom clusters were evidenced after performing a factor analysis on the BPRS-24 scores on a larger sample of 225 psychiatric patients: Disorganised cluster, including items 12 (Bizarre behaviour), 13 (Self-neglect), 14 (Disorientation), 15 (Conceptual disorganisation); Negative affect cluster, including items 16 (Blunted affect), 17 (Emotional withdrawal), 18 (Motor retardation); Positive symptoms cluster, including items 9 (Suspiciousness), 10 (Hallucinations), 11 (Unusual content of thoughts); Mania cluster, including items 7 (Mood elevation); 8 (Grandiosity), 21 (Excitement), 23 (Motion hyperactivity); Depression cluster, including items 3 (Depression), 4 (Suicidality), 5 (Guilty) and Anxiety cluster including

	Schizophrenic mean scores (SD)	Controls means scores (SD)	F (df=1,34)	p
Age (years)	37.05 (9.20)	32.87 (4.91)	2.62	0.115
Gender	14 M, 4 F	12 M, 4 F	-	-
Education (years)	12.94 (2.36)	14.25 (2.59)	2.35	0.134
Years of illness	11.5 (6.57)	-	-	-
BPRS total score	40.47 (9.92)	-	-	-
Positive cluster	4.35 (1.41)	-	-	-
Negative cluster	5.55 (1.33)	-	-	-
Depression cluster	5.27 (1.27)	-	-	-
Disorganised cluster	16.25 (4.21)	-	-	-
Mania cluster	5.88 (1.71)	-	-	-
Anxiety cluster	3.22 (1.43)	-	-	-
Raven's matrices	30.22 (2.23)	32.31 (1.92)	2.90	0.737
Eyes task	18.05 (4.68)	30.06 (3.56)	63.30	0.0001
Advanced ToM task	6.27 (5.44)	12.81 (0.40)	22.87	0.0001
Empathy quotient	36.88 (11.74)	54.75 (6.16)	29.66	0.001

Table 1: Socio-demographic, clinical and social cognition measure. Mean scores (and standard deviations) to the psychological tests separately for schizophrenic and control subjects. The significant results are highlighted by bold numbers.

items 1 (Somatic concern), 2 (Anxiety). Symptoms were assessed with regard to the month leading up to the evaluation. Both negative and positive symptoms are typical of schizophrenia but negative symptoms, especially, correlate with social cognition disorders as confirmed by various studies [27]. The participants' clinical details are reported in Table 1.

Social cognition measures

Advanced theory of mind scale: This task is an Italian adaptation of a cognitive task used by Blair and Cipolotti [28] and proposed in the literature by Happé [29]. The task consists of a short version of 13 vignettes, each accompanied by a picture and two questions; the comprehension question "Was it true, what X said?", and the justification question "Why did X say that?". The 13 story-types included Lie, White Lie, Joke, Pretend, Misunderstanding, Double Bluff and Contrary Emotion. A set of control "physical stories" was also given to the subjects. These stories did not involve mental states but described instead an unforeseen outcome with a mechanical physical cause

Empathy questionnaires (EQ): The EQ was developed because other instruments purporting to measure empathy also include items unrelated to empathy. The questionnaires were self-administered on-line, and had a forced-choice format. Participants were asked to indicate whether they "strongly agree", "slightly agree", "slightly disagree" or "strongly disagree" with a statement. The EQ comprises 40 items, with 2 points available for a "strong" response and 1 point for an appropriate "slight" response [7,30].

The Eyes Task is a revised version of the "Reading the Mind in the Eyes Test" [31]. In brief, participants are given 36 photographs depicting the ocular area in an equal number of different actors and actresses. At each corner of every photo, four complex mental state descriptors, e.g. dispirited, bored, are printed, only one of which (the target word) correctly identifies the depicted person's mental state, while the others are included as foils. The test is scored by totaling the number of items (photographs) correctly identified by the participant; therefore, the maximum

Apparatus and stimuli: Experimental paradigm: Posner's task-modified version: We modified the standard Posner cuing paradigm [20,32,33] to examine how gaze-direction cue and arrow cues guide

attention in schizophrenia and controls. Stimuli were presented using the Superlab software. Since people with schizophrenia are "concrete thinkers" (i.e. show poor abstract thought), we thought it advisable to use realistic photographs of gaze rather than schematic line drawings. Realistic cues also have the advantage of being more ecologically valid. We also wanted to see whether people with schizophrenia showed a lack (or a delay) of the normal orienting response even under ideal circumstances. We cued gaze-direction using eye shifts, rather than a turn of the head and eyes, as Langdon [34] used. In sum, the directional cues used in the present study were an image of eyes turned right or left and the neutral directional cue was of eyes looking straight forward, similar to the neutral cue used by Hietanen [35].

Participants sat 60cm from a computer monitor. Each trial began with the appearance of a central fixation point on a computer screen for duration of 700msec. After this, the subject saw indicators appear for 200ms on the computer screen of arrows or of gaze indicating the direction, left or right, followed by a point/target, which could come from the right or the left. Upon the appearance of the fixation point, the experimental subjects' eyes had to be direct and stay still for the duration of the test. The subjects were asked to indicate by pressing one of two keys on the keyboard (z corresponded to the left direction and the period symbol on the keyboard corresponded to the right direction) to indicate where they saw the target. The cues were represented by an arrow or by a real gaze that indicated where there was a probability that the stimulus appeared. The spatial cues were informative with regards the spatial location of the upcoming target. The subjects had to be aware of the exact meaning of the arrow and to press the correct keyboard key; otherwise they would not know whether and where to direct their attention. We had a third condition in which the cue gave no indication, called the neutral condition (Figure 1). Before the experiment began, participants completed practice trials until they felt confident with the task.

We saved the data collected, including the reaction time (RT), as a text file with separate columns from tables, so the data could be imported and read by SPSS statistical software. The TRs begin of the presentation of the cues (gaze or arrow) until to the response of the participants.

Results

Socio-demographic and social cognition measures

We used one-way analyses of variance (ANOVA) to compare schizophrenic and control groups regarding socio-demographic and social cognition scores.

The schizophrenic sample showed lower scores compared to the control group in all social cognition measures: in Eyes Task (p=0.0001), in the Advanced ToM Task (p=0.0001) and in the Empathy Quotient (p=0.001).

Posner's task-modified version

For the Posner's task-modified version, the time (in milliseconds) was used as a speed measure of the answers. Moreover, as an accuracy measure, we calculated the number of errors.

The reaction times means and number of errors were analysed separately with a triple interaction group X condition X cue, with the group (schizophrenics and controls) as a between factor, and conditions (valid, neutral and invalid) and cues (arrow and gaze) as repeated measures.

Reaction times results

The ANOVA showed significant main effects of the group ($F_{1,34}$=337.29; p=0.0001), conditions ($F_{1,34}$=48.63; p=0.0001) and cue ($F_{1,34}$=281.29; p=0.0001). All interaction evaluations were also significant: group x condition ($F_{1,34}$=30.98; p=0.0001), group x cues ($F_{1,34}$=257.86; p=0.0001); condition x cues ($F_{1,34}$=50.82; p=0.0001); and group x condition x cues ($F_{1,34}$=54.79; p=0.0001). These results suggest a different behaviour within the two groups of participants.

After that, we evaluated the RTs separated by cue. The ANOVA separated by the arrow cue showed the significant main effects of the group ($F_{1,34}$=4.19; p=0.043), but did not show the most significant effect of condition. The Group x Condition interaction was not significant (for means and SD see Table 2).

The ANOVA separated by the gaze cue showed the significant main effects of the group ($F_{1,34}$=434.19; p=0.0001) and conditions ($F_{1,34}$=72.71; p=0.0001). The Group x Condition interaction was also significant ($F_{1,34}$=61.557; p=0.0001).

These analyses are reported in detail in Figure 2 and Table 2.

Number of errors

The ANOVA showed significant main effects of the group ($F_{1,34}$=84.87; p=0.0001), and cue ($F_{1,34}$=29.58; p=0.0001) but not for condition. The Groups X Cue interaction was significant ($F_{1,34}$=31.94; p=0.0001). Other interactions did not showed significant effects.
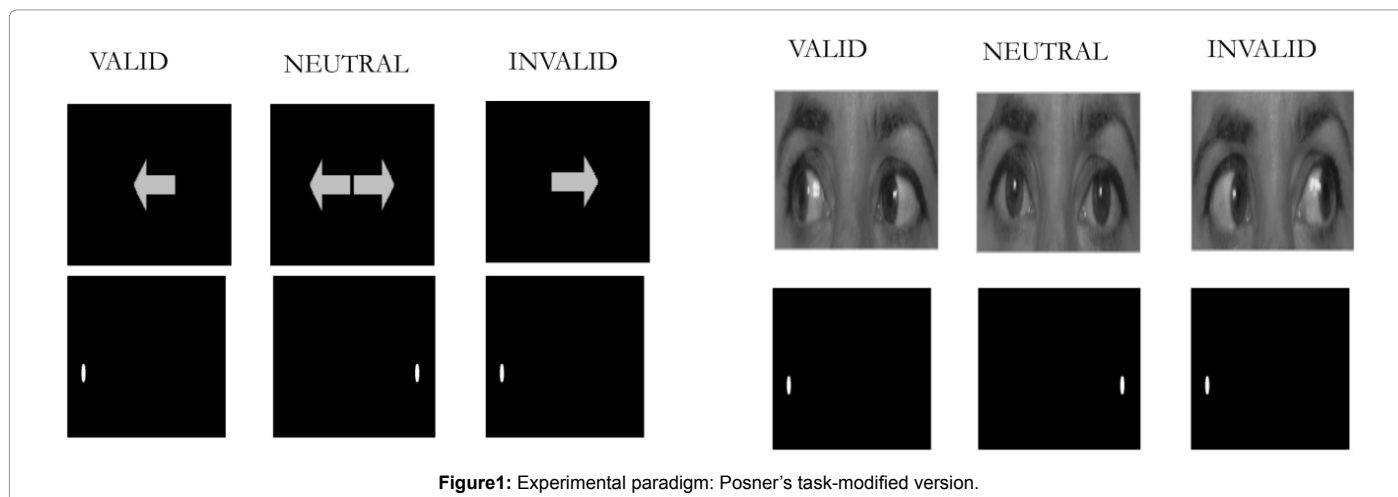

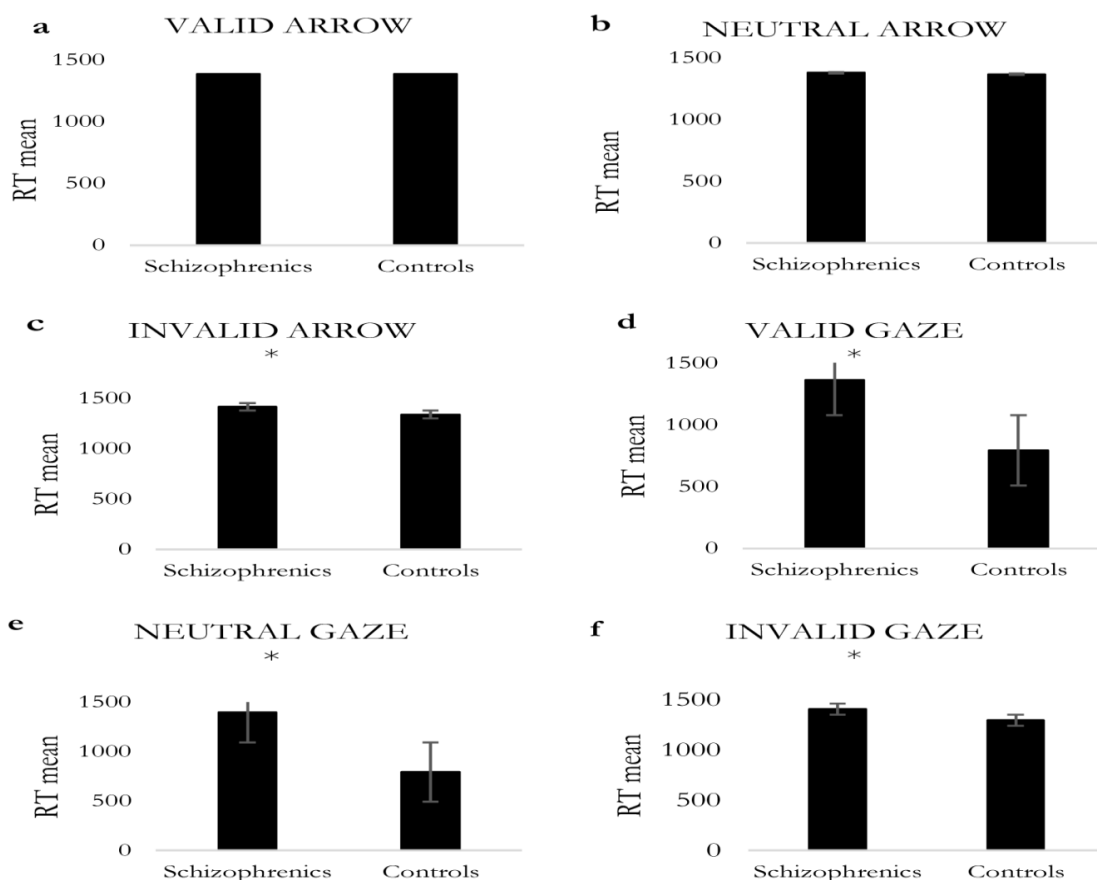**Figure1:** Experimental paradigm: Posner's task-modified version.

Figure 2: Plot of the means (and SD) of the reaction time in the experimental paradigm: Posner's task-modified version. The asterisks indicates the significant difference between groups.

	Schizophrenic Means (SD)	Controls Means (SD)	F	p
Arrow Cue				
Valid	1389.05 (76.90)	1389.91 (56.61)	0.111	0.741
Neutral	1380.57 (86.31)	1368.21 (57.76)	0.427	0.518
Invalid	1417.57 (75.60)	1340.54 (55.17)	13.721	0.001
Gaze Cue				
Valid	1363.07 (155.19)	794.61 (79.74)	173.50	0.0001
Neutral	1394.83 (340.25)	793.26 (118.17)	33.746	0.0001
Invalid	1403.21 (73.18)	1292.86 (100.54)	14.861	0.001

Table 2: Means (and SD) of the RT in the Experimental Paradigm. The significant results are highlighted by bold numbers.

After that, we evaluated the number of errors separated by cue. The ANOVA separated by the arrow cue showed significant main effects of the group ($F_{1,34}$=6.74; p=0.011), but did not show a significant main effect of Condition and Group x Condition interaction (for means and SD see Table 3).

The ANOVA separated by the gaze cue showed significant main effects of the group ($F_{1,34}$=181.29; p=0.0001), and conditions ($F_{1,34}$=4.94; p=0.009). The Group x Condition interaction was also significant ($F_{1,34}$=6.39; p=0.002 (Table 3).

These analyses are reported in Figure 3 and Table 3.

Correlation analysis

We performed a correlation analysis (Pearson coefficient) in schizophrenic group between social cognition measures (Eyes Task, Empathy Quotient and Advanced ToM) and number of errors in all conditions (valid, neutral and invalid) both gaze and arrow cue. The analysis showed a significant negative correlation between Eyes Task and number of errors in the invalid condition of gaze cue (r=-0.504, p=0.03) (Table 4).

Discussion

The study used a modified Posner paradigm to examine how gaze-direction cues and arrow cues guide attention in subjects with schizophrenia and matched controls.

In the current study, the results showed that schizophrenia subjects were slower and less accurate when the cue was the gaze rather the arrow.

Specifically, when the arrow represented the condition the schizophrenic patients had the same behaviour as the healthy subjects. The result obtained from the analysis of the RTs was confirmed from the analysis made on the number of errors. The schizophrenic subjects did not show a significantly number of errors different from the healthy subjects when the cue was represented by the arrow. Instead, the performance of the schizophrenics was compromised when the cue was the gaze. In the schizophrenics the benefit reduction for the gaze
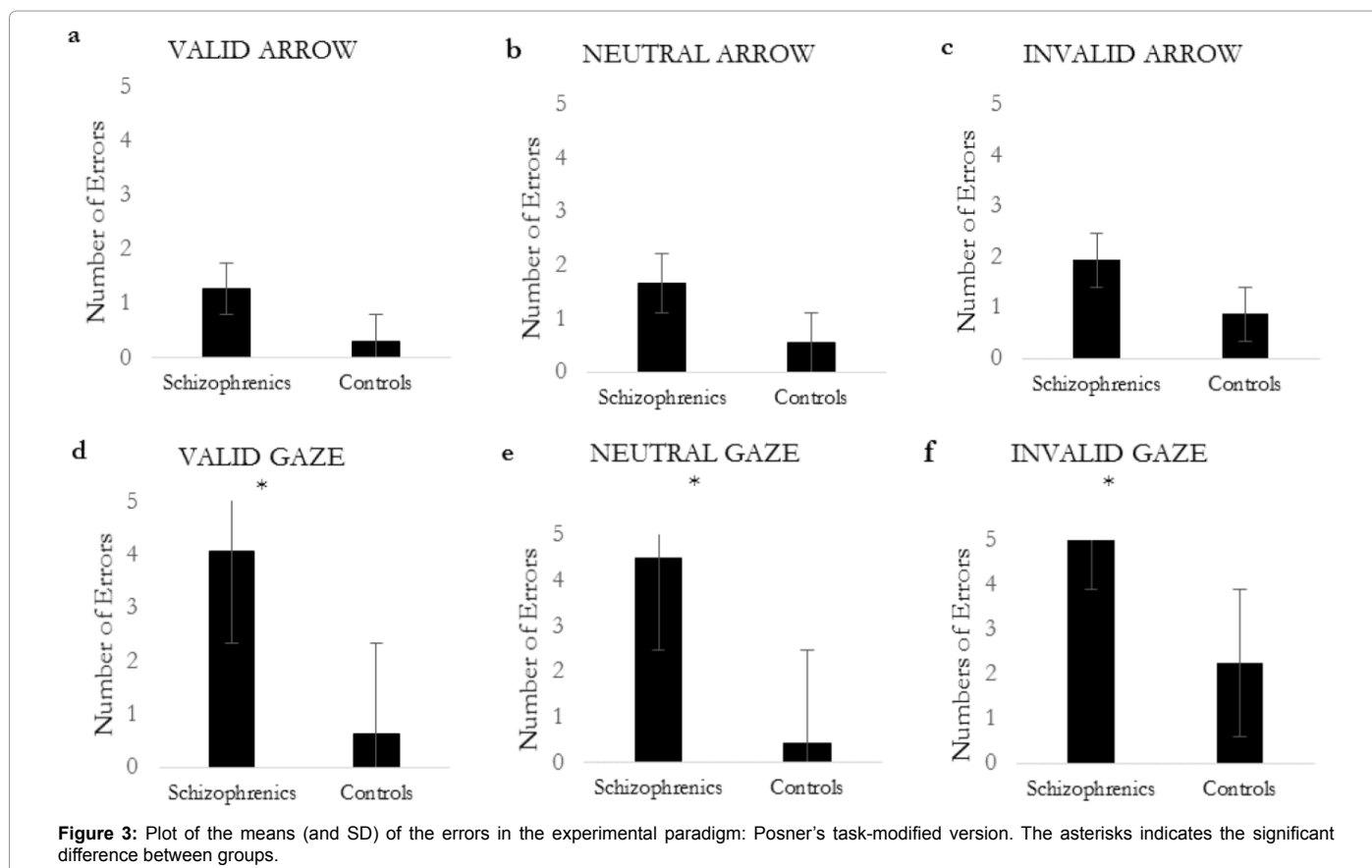
Figure 3: Plot of the means (and SD) of the errors in the experimental paradigm: Posner's task-modified version. The asterisks indicates the significant difference between groups.

	Schizophrenic Means (SD)	Controls Means (SD)	F	p
Arrow Cue				
Valid	1.27 (2.46)	0.31 (0.60)	2.316	0.138
Neutral	1.66 (2.40)	0.56 (1.09)	2.850	0.101
Invalid	1.94 (3.07)	0.87 (0.80)	1.816	0.187
Gaze Cue				
Valid	4.61 (2.09)	0.62 (0.95)	48.926	0.0001
Neutral	4.50 (3.88)	0.43 (0.62)	17.046	0.0001
Invalid	5.56 (2.25)	2.25 (0.81)	71.833	0.0001

Table 3: Means (and SD) of the errors in the experimental paradigm. The significant results are highlighted by bold numbers.

	Eyes Task	E.Q.	ToM
Arrow			
Valid	-0.068	0.182	0.318
Neutral	-0.228	0.136	0.296
Invalid	-0.147	0.189	0.408
Gaze			
Valid	0.026	-0.107	0.144
Neutral	-0.17	0.209	0.405
Invalid	-0.504*	-0.202	0.298
*p<0.005			

Table 4: Correlation analysis in schizophrenic group between social cognition measures and number of errors in all conditions both gaze and arrow cue.

cue was not attributable to an attention deficit, but more likely linked to a failure in processing the social information from the gaze-direction. Our data are indicative of a gaze hyposensivity in schizophrenic subjects.

Our results were in contrast with Langdon and coll's research [10] in which their schizophrenic patients showed a hypersensivity e to gaze cues. It is important to highlight that in the Langdon 's study [10] the cue was represented by a head turned right, left, up, or down and the participants were ask to detect targets. Thus, Longdon's participants did not really visualize the orienting of gaze.

The results for the control group were different from those for the schizophrenic. When the cue was represented by gaze the controls halved their RTs. Thus, they benefit from the gaze cue.

Regarding the three condition, i.e. valid, neutral and invalid, both groups were penalized when the position of both cues are invalid compared to the target position.

Previous studies on the orienting-of-attention ability in a healthy sample [19] have investigated this cognitive process using the classic task of attention orientation made by Posner [20]. In Posner's classic task, the participants' reaction times were faster when the stimulus was a point in space where its probability of occurrence was high (valid condition), but they were slower when the stimulus appeared at a point where the probability of occurrence was low (invalid condition). The reactions times had intermediate values if the subject had no information on the probability of occurrence of the stimulus (neutral condition). Our results confirm the previous studies' findings [20,33,36]. In fact, both groups showed higher reaction times in the invalid condition compared to the other two conditions (valid and neutral).

The difference of the schizophrenic sample's performance between the arrow and gaze cues, compared to the control group, allows us to talk of "social attention" impairment in this psychiatric disorder [5,37]. Social attention has increasingly been seen as disrupted in schizophrenia [37,38] and these disturbances are now often understood within a wider context of disease-related impairments in social motivation and functioning [13,39]. This distinct form of attention was generally framed in reference to social cognition, which in turn has been defined as a complex set of representations of internal bodily states, knowledge of self, perception of others, and interpersonal motivations [1]. This evidence is confirmed by the result obtained in our correlation analysis, in which the gaze cue in invalid condition negatively correlates with the Eyes Task in subjects with schizophrenia. This means that the lower the score is in the Eyes Task the greater the difficulty of these subjects is to direct their attention toward the target when the social cue provides the wrong information. This confirms the relationship between the interpretation of the gaze of other people and the ability to use this information to direct the attention to the target. From the first days and weeks of life, infants orient the attention toward the caregiver. In particular, they prefer to look at people rather than at things, and when they are looking at people, they look at their eyes. They even when prefer to look at people who are looking at them rather than people who are looking away. Thus, parents look at their babies. This mechanism is of importance to the emergence of social mind [40]. Infants soon learn, even before they can speak, that they can exploit attention in order to get things they want. Indeed, they also learn to follow the gaze of other people. Such sharing of attention would seem critical for the maintenance of normal social cognition. Gaze is pivotal in social interaction in that it enables us to decipher the inner thoughts of other people from the direction of their attention. The social inadequacy often seen in patients suffering from chronic schizophrenia might, in part, be attributable to the compromise in gaze cognition such as demonstrated in the current study. A deeper understanding of the symptoms related to gaze in schizophrenia might offer some strategy to rescue these people from their social isolation.

Survival can depend on the ability to change a current course of action to respond to potentially advantageous or threatening stimuli. Our findings are consistent with the view that schizophrenia is characterised by abnormalities of social cognition ability coupled with a general impairment of the attention process. In particular, we believe that social attention deficit depends on social cognition impairment.

Previous studies have used gaze cues embedded in a face stimulus to signal the location of an target [22,37]. The face is a complex stimulus. Numerous studies have demonstrated that face perception is multi-faceted [41]: not only do we recognize individuals, but also monitor their faces to obtain a continuous stream of social information, ranging from communicative gestures to emotional and attentive states. For this reason, in our study compared to previous studies, we decided to use just gaze cues. In fact, the gaze provides insight into an individual's attentive state, including their level of engagement, intentions, or focus of interest. Indeed, human infants primarily use the orientation of the eyes, rather than the head, to determine another's direction of gaze [42]. Gaze interplay is a salient feature of social interaction and is abnormal in a number of psychiatric conditions, in which patients typically avoid looking into the eyes of others. These data suggest the importance to implement the gaze component in rehabilitation treatment, which should be directly demonstrated by future studies. Indeed, considering the pivotal role played by gaze detection and interpretation in the development of social cognition, gaze interpretation ability can be regarded as an important part of the rehabilitation strategies for schizophrenic people. Learning about this ability would allow them to interpret important social signals and to interact correctly with other people.

According to Ciccone et al. [43] in the rehabilitation treatment is important involve care managers into the health care system to support general practitioners and specialists in the management of patients. Future studies should consider the possibility of incorporating a patient empowerment model which considers the patient as the most important member of the health team and care managers as key health care collaborators able to enhance and support services to patients provided by physicians in the primary health care system.

In conclusion, the deficit of one's ability to orient one's attention to a social cue could be derived from social cognitive impairment in schizophrenia subjects and not be due to an attentional deficit. As a matter of fact the small sample group is an important limitation to our study.

References

1. Mazza M, Giusti L, Albanese A, Mariano M, Pino MC, et al. (2012) Social cognition disorders in military police officers affected by posttraumatic stress disorder after the attack of An-Nasiriyah in Iraq 2006. Psychiatry Research 198: 248-52.

2. Millan MJ, Bales KL (2013) Towards improved animal models for evaluating social cognition and its disruption in schizophrenia: the CNTRICS initiative. Neurosci Biobehav Rev 37: 2166-2180.

3. Ventura J, Wood RC, Jimenez AM, Hellemann GS (2013) Neurocognition and symptoms identify links between facial recognition and emotion processing in schizophrenia: meta-analytic findings. Schizophrenia Research 151: 78-84.

4. Mazza M, Lucci G, Pacitti F, Pino MC, Mariano M, et al. (2010). Could schizophrenic subjects improve their social cognition abilities only with observation and imitation of social situations? Neuropsychologycal Rehabilitation 20: 675-703.

5. Schwartz BL, Vaidya CJ, Howard JH, Deutsch SI (2010) Attention to gaze and emotion in schizophrenia. Neuropsychology 24: 711-720.

6. Tso IF, Carp J, Taylor SF, Deldin PJ (2014) Role of visual integration in gaze perception and emotional intelligence in schizophrenia. Schizophr Bull 40: 617-625.

7. Baron-Cohen S, Wheelwright S (2004) The empathy quotient: An investigation of adults with Asperger syndrome or high functioning autism, and normal sex differences. Journal of Autism Development Disorders 34: 163-175.

8. Sodian B, Thoermer C (2008) Precursors to a theory of mind in infancy: perspectives for research on autism. Q J Exp Psychol (Hove) 61: 27-39.

9. Akiyama T, Kato M, Muramatsu T, Maeda T, Hara T, et al. (2008) Gaze-triggered orienting is reduced in chronic schizophrenia. Psychiatry Res 158: 287-296.

10. Langdon R, Corner T, McLaren J, Coltheart M, Ward PB (2006) Attentional orienting triggered by gaze in schizophrenia. Neuropsychologia 44: 417-429.

11. Dalmaso M, Galfano G, Tarqui L, Forti B, Castelli L (2013) Is social attention impared in schizophrenia? Gaze, but not pointing gestures, is associated with spatial attention deficits. Neuropsychology 27: 608-613.

12. Adolphs R (2001) The neurobiology of social cognition. Curr Opin Neurobiol 11: 231-239.

13. Burns JK (2004) An evolutionary theory of schizophrenia: cortical connectivity, metarepresentation, and the social brain. Behav Brain Sci 27: 831-855.

14. Magne MJ, Kahn RS, Cahn W, Kemner C (2011) More prolonged brain activity related to gaze cueing in schizophrenia. Clin Neurophysiol 122: 506-511.

15. von dem Hagen EA, Stoyanova RS, Rowe JB, Baron-Cohen S, et al. (2014) Direct Gaze Elicits Atypical Activation of the Theory-of-Mind Network in Autism Spectrum Conditions. Cerebral Cortex 24: 1485-1492.

16. Macrae CN, Hood BM, Milne AB, Rowe AC, Mason MF (2002) Are you looking at me? Eye gaze and person perception. Psychol Sci 13: 460-464.

17. Vuilleumier P (2005) Cognitive science: staring fear in the face. Nature 433: 22-23.

18. Golan O, Baron-Cohen S, Golan Y (2008) The 'Reading the Mind in Films' Task -child version-: complex emotion and mental state recognition in children with and without autism spectrum conditions. Journal of Autism Development Disorders 37: 1096-1106.

19. Ristic J, Friesen CK, Kingstone A (2002) Are eyes special? It depends on how you look at it. Psychon Bull Rev 9: 507-513.

20. Posner MI (1980a) Orienting of attention. Quarterly Journal of Experimental Psychology 32: 3-25.

21. Ricciardelli P, Driver J (2008) Effects of head orientation on gaze perception: how positive congruency effects can be reversed. Q J Exp Psychol (Hove) 61: 491-504.

22. Bonifacci P, Ricciardelli P, Lugli L, Pellicano A (2008) Emotional attention: effects of emotion and gaze direction on overt orienting of visual attention. Cogn Process 9: 127-135.

23. American Psychiatric Association (2000) Diagnostic and Statistical Manual of Mental Disorders, (4th edn) APA, Washington, DC.

24. Kessler KA, Waletzky JP (1981) Clinical use of the antipsychotics. Am J Psychiatry 138: 202-209.

25. Raven JC (1938) Progressive matrices: A perceptual test of intelligence. London 7 H.K. Lewis.

26. Roncone R, Ventura J, Impallomeni M, Falloon IR, Morosini PL, et al. (1999) Reliability of an Italian standardized and expanded Brief Psychiatric Rating Scale (BPRS 4.0) in raters with high vs. low clinical experience. Acta Psychiatrica Scandinavica 100: 229-236.

27. Mazza M, De Risio A, Surian L, Roncone R, Casacchia M (2001) Selective impairments of theory of mind in people with schizophrenia. Schizophr Res 47: 299-308.

28. Blair RJ, Cipolotti L (2000) Impaired social response reversal. A case of 'acquired sociopathy'. Brain 123 : 1122-1141.

29. Happé FG (1994) An advanced test of theory of mind: understanding of story characters' thoughts and feelings by able autistic, mentally handicapped, and normal children and adults. Journal of Autism Development Disorders 24: 129-54.

30. Baron-Cohen S, Wheelwright S, Skinner R, Martin J, Clubley E (2001) The autism spectrum quotient (AQ): Evidence from Asperger syndrome/high-functioning autism, males and females, scientists and mathematicians. Journal of Autism Development Disorders 31: 5-17.

31. Baron-Cohen S, Wheelwright S, Hill J, Raste Y, Plumb I (2001) The "Reading the Mind in the Eyes" Test revised version: a study with normal adults, and adults with Asperger syndrome or high-functioning autism. J Child Psychol Psychiatry 42: 241-251.

32. Posner MI, Early TS, Reiman E, Pardo PJ, Dhawan M (1988) Asymmetries in hemispheric control of attention in schizophrenia. Arch Gen Psychiatry 45: 814-821.

33. Posner MI, Snyder CR, Davidson BJ (1980) Attention and the detection of signals. J Exp Psychol 109: 160-174.

34. Langdon R, Coltheart M (1999) Mentalising, schizotypy, and schizophrenia. Cognition 71: 43-71.

35. Hietanen JK (1999) Does your gaze direction and head orientation shift my visual attention? Neuroreport 10: 3443-3447.

36. Carrasco M (2009) Cross-modal attention enhances perceived contrast. Proc Natl Acad Sci U S A 106: 22039-22040.

37. Nestor PG, Klein K, Pomplun M, Niznikiewicz M, McCarley RW (2010) Gaze cueing of attention in schizophrenia: individual differences in neuropsychological functioning and symptoms. J Clin Exp Neuropsychol 32: 281-288.

38. Sasson N, Tsuchiya N, Hurley R, Couture SM, Penn DL, et al. (2007) Orienting to social stimuli differentiates social cognitive impairment in autism and schizophrenia. Neuropsychologia 45: 2580-2588.

39. Hoffman RE, Varanko M, Gilmore J, Mishara AL (2007) Experiential features used by patients with schizophrenia to differentiate 'voices' from ordinary verbal thought. Psychological Medicine 38: 1167-1176.

40. Jones W, Klin A (2013) Attention to eyes is present but in decline in 2-6-month-old infants later diagnosed with autism. Nature 504: 427-431.

41. Leopold DA, Rhodes G (2010) A comparative view of face perception. J Comp Psychol 124: 233-251.

42. Tomasello M, Hare B, Lehmann H, Call J (2007) Reliance on head versus eyes in the gaze following of great apes and human infants: the cooperative eye hypothesis. J Hum Evol 52: 314-320.

43. Ciccone MM, Aquilino A, Cortese F, Scicchitano P, Sassara M, et al. (2010). Feasibility and effectiveness of a disease and care management model in the primary health care system for patients with heart failure and diabetes (Project Leonardo). Vascular Health and Risk Management 6: 297-305.