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Activation of brain areas concerned with social cognition during moral decisions is abnormal in schizophrenia patients and unaffected siblings

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ABSTRACT

Moral decision-making involves complex social cognitive processes which are known to be altered in patients with schizophrenia and first-degree relatives. Traditional philosophical views on human moral behavior have distinguished between utilitarian views (which emphasize outcomes) and deontological approaches (defining what is right to do according to certain norms). Since emotions have been suggested to play a determining role in moral behavior, we hypothesized patients with schizophrenia and unaffected siblings would make more utilitarian choices and show faulty activation of brain areas concerned with emotion regulation during such tasks. Unexpectedly, all participants ($n = 13$ per group) made the same proportion of utilitarian and deontological decisions. Brain activation common to all groups induced by moral decisions included two circumscribed portions of right ventromedial and dorsolateral prefrontal cortex, adding to previous evidence on a right prosencephalic cognitive network involved in ethical decisions. However, brain activation induced by moral decisions was different in healthy persons, schizophrenia patients, and nonpsychotic siblings in regards to areas directly concerned with emotion processing. These results seem to underscore the role of acquired norms in moral decisions, a frequently overlooked concept in the neurobiological characterization of human ethical behavior, and add to previous evidence of abnormal social cognitive processing in schizophrenia.
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1. Introduction

Schizophrenia is defined by the presence of delusions, hallucinations, formal thought disorder, and negative symptoms (American Psychiatric Association, 1994), in addition to neurocognitive, emotion processing, and social cognitive deficits, which are in part inherited and therefore shared by first-degree relatives of patients (de Achával et al., 2010). More complex forms of human interaction in schizophrenia, involving moral decision-making, have received very little attention in the literature (Baruk and Amiel, 1953; Johnson, 1960), with only one recent communication on the topic (Wischniewski and Brüne, 2011). Functional magnetic resonance imaging has become a prominent method of exploration of brain systems in schizophrenia (Gur and Gur, 2010). In particular, different abnormalities of brain activation related to emotion processing and social cognitive tasks have been found in patients with schizophrenia, underlying deficits of actual functioning in these areas (see Gur and Gur, 2010 for a review; de Achával et al., 2012). However, to our knowledge no study has addressed brain activation during moral decision-making in schizophrenia, which has been proposed to be closely related to affective and social cognitive

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processing (Greene et al., 2001; Young et al., 2010a), known to be prominently disturbed in this disorder (see Gur and Gur, 2010 for a review; de Achával et al., 2010; de Achával et al., 2012). Whereas patients with schizophrenia and unaffected first-degree relatives share several social cognitive deficits (de Achával et al., 2010), the presence of abnormalities of moral decision in first-degree relatives of schizophrenia patients have not been reported to our knowledge. Exploring this issue would permit to make inferences on the influence of genetic predisposition to schizophrenia in this regard.

Apart from its importance for further characterization of complex social phenomena in schizophrenia, the study of moral decision-making in siblings discordant for the disease might represent a model to probe the role of emotion processing and social cognition in moral decision-making in general. Traditional philosophical and psychological views on how human beings decide on moral affairs (Piaget, 1965; Turiel, 1983) place emphasis on the role of reasoning, usually in the form of either following certain universal moral rules (i.e., deontological approaches, Kant, 1785, 2004), or the attainment of pleasure and well-being and avoidance of pain (i.e., utilitarian approaches, Bentham, 1907; Mitsis, 1988), or a combination of the two. More recently, some philosophers have proposed that emotions can also play a significant moral role (Blum, 1994; Nussbaum, 1978). There is recent neuroscientific evidence to support such a view (Greene et al., 2001; Haidt, 2001; Damasio, 2007), though experimental data have not been uniform regarding the precise role of emotions in ethical behavior (Nichols and Mallon, 2006). Emotions have been proposed to play a key role in moral decision making in two main contexts. First, a brain emotion processing system integrated at the ventromedial prefrontal cortex (VMPFC) has been posited to be critical to identifying an unsuccessful intent to cause harm as less morally acceptable than actual harm caused by accident (Ciaramelli et al., 2007; Mendez et al., 2005; Young et al., 2010a). Second, the reason why inducing direct personal harm to prevent greater damage is morally less acceptable than indirect personal loss to provoke the same, utilitarian outcome, is believed to be because the former situation evokes a greater emotional response (Greene, 2007). In both cases, it is proposed that faulty emotional processing is causally related to the choice of utilitarian options when faced with moral dilemmas. According to this model, moral actions that result in personal damage are more salient from an emotional perspective and, in this way, affect people's judgment (Greene et al., 2001), even though support for the role in moral judgment of the brain network traditionally considered to subserve emotion and affective processing has not been uniform (Nichols and Mallon, 2006; Baumgartner et al., 2011). The extensive documentation of abnormal emotional processing and social cognitive abilities in patients with schizophrenia makes this group apt to test the role of emotions in moral decision-making. Thus, in order to test the hypothesis that faulty emotional processing results in a tendency to make utilitarian-type responses to moral dilemmas, and to characterize the neural bases for such difference, we compared healthy individuals to patients with schizophrenia, predicting the latter would show a different pattern of moral decision-making and abnormal brain activation induced by ethical dilemmas. To avoid the confounding effects of medications and active psychotic symptoms, we also tested unmedicated, nonpsychotic siblings of schizophrenia patients, who share substantial emotion processing deficits with them (de Achával et al., 2010; de Achával et al., 2012). An additional reason for studying nonpsychotic siblings of patients with schizophrenia is to determine if observed abnormalities are heritable (Preston and Weinberger, 2005). Quantitative biological traits (including patterns of brain activation as revealed by functional MRI) which are shared by patients and unaffected siblings are usually referred to as intermediate phenotypes. A preliminary finding of overlapping abnormalities of brain activation induced by moral decision-making would suggest this might represent an intermediate phenotype, as it has been found in other social cognitive paradigms (Preston and Weinberger, 2005; Gur and Gur, 2010; de Achával et al., 2012). We predicted that patients with schizophrenia and unaffected siblings would make more utilitarian vs. deontological judgments on the basis of faulty emotional processing, as suggested by prior studies (Baruk and Amiel, 1953; Johnson, 1960), and that they would display faulty activation of predominantly right ventromedial prefrontal cortex (Young and Koenigs, 2007), insula, temporoparietal junction, and anterior cingulate (Sanfey et al., 2003; Young et al., 2010b; de Achával et al., 2012) when confronted with ethical dilemmas. We also reasoned that activation of such areas in the experimental groups would be more divergent from the normal pattern when moral decisions attained by participants were utilitarian (i.e., those predicted to be more characteristic of experimental groups) instead of deontological.

2. Methods and materials

2.1. Participants

Two psychiatrists (SMG, EYC) and a psychologist (DdA) assessed all participants, who were seen at the Cognitive Neurology Section and the Psychiatry Department at FLENI Hospital, Buenos Aires. All participants were right-handed and provided written informed consent as approved by the local bioethics committee, in accordance with the ethical standards set by the 1964 Declaration of Helsinki. A family member of patients was also requested to provide written consent.

2.1.1. Patients

Outpatients at the Departments of Neurology and Psychiatry (Table 1) were invited to participate in the study if they (a) fulfilled DSM-IV-TR diagnosis of schizophrenia, any subtype, confirmed with a Composite International Diagnostic Interview (Robins et al., 1988) administered by a consultant psychiatrist (EYC), (b) were aged 18–50 years, and (c) had been on the same medication plan for at least two weeks. Exclusion criteria were (a) use of illegal substances in the previous 6 months, (b) active symptoms having recently (<2 weeks) warranted antipsychotic dose adjustment or admission to the hospital, day hospital, or intensive outpatient treatment, or (c) a history of mental retardation. Current symptom severity was assessed with the Positive and Negative Syndrome Scale (Kay et al., 1987).

2.1.2. Siblings

Siblings (Table 1) were recruited from families of patients participating in this study ($n = 7$), and from families with affected members who did not fulfill the symptom stability criterion ($n = 6$). Exclusion criteria included (a) use of illegal substances in the previous 6 months (b) the lifetime presence of any DSM-IV-TR Axis I psychotic disorder diagnosis as detected by a psychiatric interview with the consultant psychiatrist (EYC) and (c) a medication history of antipsychotics, antidepressants, or mood stabilizers. Siblings were not found to have experienced Axis I Mood and Anxiety disorders in the clinical interview.

2.1.3. Controls

Healthy comparison individuals (Table 1) were recruited from the local community. Exclusion criteria included (a) use of illegal substances in the previous 6 months (b) the lifetime presence of any DSM-IV-TR Axis I anxiety, mood, or psychotic disorder diagnosis as detected by a psychiatric interview with a psychiatrist (EYC) and (b) a medication history of antidepressants, antipsychotics, or mood stabilizers.

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