Violent persons with schizophrenia and comorbid disorders: A functional magnetic resonance imaging study

C.C. Joyal a,b,c,⁎, A. Putkonen a, A. Mancini-Marie c, S. Hodgins d, M. Kononen e, L. Boulay e, M. Pihlajamaki e, H. Soininen f, E. Stip c, J. Tiihonen a,g, H.J. Aronen h

a Niuvanniemi Hospital, Kuopio, Finland
b Philippe-Pinel Institute of Montreal, Canada
c Fernand-Seguin Research Center, L-H Lafontaine Hospital, Montreal, Canada
d Department of Forensic Mental Health Science, Institute of Psychiatry, King’s College London, United Kingdom
e Department of Radiology, University of Kuopio, Finland
f Department of Neurology, Kuopio University Hospital, Kuopio, Finland
g Department of Clinical Physiology, Kuopio University Hospital, Kuopio, Finland
h fMRI Center, University of Helsinki, Finland

Received 4 May 2006; received in revised form 7 December 2006; accepted 11 December 2006
Available online 7 February 2007

Abstract

The main goal of this functional Magnetic Resonance Imaging (fMRI) study was to verify the hypothesis that seriously violent persons with Sz and the co-morbid diagnoses of an Antisocial Personality Disorder (APD) and a Substance Use Disorder (Sz+APD+SUD) would present a different pattern of prefrontal functioning than seriously violent persons with Sz only. In support with the main hypothesis, frontal basal cortices were significantly less activated in persons with Sz+APD+SUD during the execution of a go/no-go task than in persons with Sz only and non-violent persons without a mental illness. In contrast, significantly higher activations in frontal motor, premotor and anterior cingulate regions were observed in the Sz+APD+SUD group than in the Sz-only group.

© 2007 Elsevier B.V. All rights reserved.

Keywords: Schizophrenia; Violence; Antisocial personality disorder; fMRI

1. Introduction

Although the vast majority of persons with schizophrenia (Sz) are clearly not aggressive (e.g. Monahan et al., 2001), subgroups of patients are at significantly higher risks for interpersonal violence than persons without a mental illness (e.g. Arseneault et al., 2000; Brennan et al., 2000; Hodgins et al., 2003; Tiihonen et al., 1997; Wallace et al., 2004; Walsh et al., 2002; Joyal et al., in press for a review). The link between schizophrenia and violence for these subgroups is poorly understood, however, as it is heterogeneous. While violent persons with Sz are commonly viewed as suffering from more neurological dysfunction and presenting poorer neuropsychological capacities than non-violent persons with
Sz (e.g. Barkataki et al., 2005; Krakowski et al., 1989; Volavka, 2002; Kumari et al., 2006), the opposite might characterize community offenders with a history of antisocial behaviors that antedate the onset of Sz (Lapierre et al., 1995; Hodgins, 2000; Joyal et al., 2003; Potvin et al., 2006; Stirling et al., 2005). Naudts and Hodgins (2006) recently suggested that men with Sz and a history of antisocial behaviors might present neural dysfunction at the basal and orbital levels of the frontal lobes, a neurological pattern more closely associated with APD and lower-order executive dysfunctions such as impulsivity than with Sz. In order to investigate this hypothesis, fMRI was used with violent offenders with Sz while they performed a simple go/no-go paradigm, known to induce inferior frontal cortex activation.

2. Methods

Due to space limitation, details of standard technical procedures used for this study are available online (https://oraprdnt.uqtr.uquebec.ca/pls/public/gscw031?owa_no_site=409&owa_no_fiche=8&owa_aperc=N&owa_no_fiche_dev_ajout=&owa_no_fiche_dev=_suppr_=1E1). Briefly, 36 participants were recruited; they were all right-handed, noncolor-blind, male Caucasians aged between 28 and 54. Among them, 24 were homicide offenders with a primary diagnosis of schizophrenia, paranoid subtype (from Putkonen et al., 2004), who either received the diagnoses of Sz+APD+SUD (n=12; whose assault resulted from an unplanned altercation with a friend in a context of alcohol abuse; Joyal et al., 2004) or the sole diagnosis of Sz (n=12; Sz-only; no history of violence and judged to have assaulted in response to a psychotic manifestation; Joyal et al., 2004). In addition, 12 non-criminal men screened for psychiatric diagnosis constituted the control group (C).

The behavioral task was a computerized go/no-go paradigm developed for fMRI sessions at Giessen University (Germany). The go/no-go task engages the orbital cortex (p.ex. Horn et al., 2003) and inferior or medial frontal gyri when performed by healthy volunteers (e.g. Watanabe et al., 2002), especially in the right hemispheres (e.g. Garavan et al., 1999; Rubia et al., 2003). It is also used in fMRI study of clinical population presenting impulsivity and fronto-orbital dysfunction (e.g. Altshuler et al., 2005). The task is described in further details in our website (see the address above). Acquisition and analyses of the data were based on approaches previously used by members of our group (e.g. Fahim et al., 2005; Pihlajamaki et al., 2005; detailed in our website). Subtractions were obtained between brain activation during the cognitive condition (go or no-go depending on the context; complex reaction time) minus the reference condition (go systematically; simple reaction time). Both a priori hypothesis-driven and exploratory whole-brain analyses were performed. The a priori search strategy included the following prefrontal regions of interest: BA (Brodmann Areas) 9, 10, 11, 44, 45, 46, and 47. Small volume correction and box volume function were used with a probability threshold corrected for multiple comparisons ($p_{\text{corr}}<0.05$ in SPM2 and $p_{\text{corr}}<0.001$ for the exploratory search). Within-group and between-group comparisons were performed. It was specifically hypothesized that among the patients, significantly lower frontal activation would be found at the basal and orbital levels while significantly higher activation would be generated in other parts of the frontal cortex.

Table 1
BOLD cerebral activation during cognitive minus reference conditions: within-group R.O.I. search

<table>
<thead>
<tr>
<th>Group</th>
<th>Prefrontal region</th>
<th>L/R</th>
<th>BAz</th>
<th>TAL</th>
<th>$V$</th>
<th>$Z$</th>
<th>$p^*$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td>Middle frontal gyrus</td>
<td>R</td>
<td>46</td>
<td>48 33 26</td>
<td>29</td>
<td>3.87</td>
<td>0.002</td>
</tr>
<tr>
<td></td>
<td>Middle frontal gyrus</td>
<td>R</td>
<td>45/9</td>
<td>50 31 29</td>
<td>169</td>
<td>4.05</td>
<td>0.010</td>
</tr>
<tr>
<td></td>
<td>Middle frontal gyrus</td>
<td>R</td>
<td>46</td>
<td>45 53 11</td>
<td>36</td>
<td>3.43</td>
<td>0.058#</td>
</tr>
<tr>
<td></td>
<td>Middle frontal gyrus</td>
<td>R</td>
<td>47</td>
<td>53 10 16</td>
<td>3.45</td>
<td>0.059#</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Orbitofrontal cortex</td>
<td>R</td>
<td>48</td>
<td>53 10 16</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Superior frontal gyrus</td>
<td>L</td>
<td>10</td>
<td>-18 53 3</td>
<td>59</td>
<td>3.29</td>
<td>0.047</td>
</tr>
<tr>
<td></td>
<td>Inferior frontal gyrus</td>
<td>L</td>
<td>11</td>
<td>-53 13 19</td>
<td>18</td>
<td>2.97</td>
<td>0.034</td>
</tr>
<tr>
<td></td>
<td>Middle superior frontal gyrus</td>
<td>R</td>
<td>9</td>
<td>10 24 14</td>
<td>28</td>
<td>2.99</td>
<td>0.050</td>
</tr>
<tr>
<td></td>
<td>Middle frontal gyrus</td>
<td>R</td>
<td>47</td>
<td>34 47 27</td>
<td>2.80</td>
<td>0.058#</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Inferior frontal gyrus</td>
<td>L</td>
<td>10</td>
<td>49 35 4</td>
<td>2.76</td>
<td>0.015</td>
<td></td>
</tr>
</tbody>
</table>

R.O.I.: Region Of Interest; TAL: Talairach coordinates; L: left; R: right, BA: Brodmann area; $V$: voxels; $Z$: z score; *corrected for multiple comparisons; #approaching significance; Sz+PD+SUD: Schizophrenia+Antisocial Personality Disorder+Substance Use Disorder; Sz-only: Schizophrenia Only.
cortex in the Sz+APD+SUD subgroup compared with the Sz-only subgroup.

3. Results

The within-group analyses for prefrontal regions first revealed that among healthy participants, the cognitive condition of the task induced significantly higher activation in lateral (BA45/9 and BA46) and basal (BA11) cortices, with elevated activation at the anterior medial pole (BA10) and orbital (BA47) frontal areas approaching significance ($p<0.058$ and $p<0.059$, respectively), all in the right hemisphere (Table 1 and Fig. 1). In the Sz+APD+SUD group, the same cognitive condition elicited significantly higher activations in anterior and lateral frontal regions (BA10 bilaterally and the left BA44/45), with higher activation in the right BA9 approaching significance ($p=0.0058$; Table 1). In the Sz-only group, two significant frontal loci of activation were observed, in the left inferior frontal gyrus (BA10) and orbitofrontal cortex (BA47; Table 1).

Between-group comparisons for prefrontal regions revealed that activation in the middle frontal gyrus (BA46/9) in the control group was significantly higher than that of both study groups (Table 2). In addition, the frontal orbital (BA47) and a locus of the middle frontal gyrus (BA45) were significantly more activated in the control group than in the Sz+APD+SUD group (Table 2). In the Sz-only group, significant BOLD signals were also found in diverse regions of the inferior frontal gyrus and the orbital cortex compared with the Sz+APD+SUD group (Table 2). No prefrontal activation was significantly higher in the study groups compared with the controls.

Exploratory, whole-brain between-group comparisons shown significantly lower activations in different areas for both study groups compared with the controls (Table 3). Significantly higher activations were found in both study groups compared with the controls in the superior temporal gyrus. Hyperactivations emerged for the Sz+APD+SUD group in regions BA 4, BA 6, and BA 24 (anterior cingulate gyrus) compared with the controls and the Sz-only subgroup. Areas within the
fusiform gyrus (BA 36), the inferior parietal cortex (BA 40), and the cerebellum were also found to be significantly more activated in the Sz+APD+SUD than in the Sz-only group.

4. Discussion

In this fMRI study, homicide offenders with Sz, with or without additional diagnoses of APD and SUD were...
compared with non-criminal men during the execution of a go/no-go task. Three main findings emerged: 1) only the Sz+APD+SUD group failed to show higher blood flow in the orbital (BA 47) or basal (BA 11) regions during the cognitive part of the task; 2) between-group comparisons confirmed that activations in the inferior or the orbital part of the prefrontal cortex were significantly higher in both the controls and the Sz-only group compared with the Sz+APD+SUD group and; 3) other frontal regions were significantly more activated in the Sz+APD+SUD group than in the Sz-only group (BA 4, BA 6 and BA 24). These results could not simply be attributed to different capacities to perform the task because behavioral performances were similar between the groups. Thus, the possibility remains that better frontal functioning outside the basal regions would be found in violent persons with Sz+APD+SUD compared with violent persons with Sz-only, although future investigations are warranted.

Overall, the present results concord with the hypothesis that violent persons with Sz and a long history of antisocial behaviors might suffer from neural dysfunction affecting basal or orbital parts of the prefrontal cortex (Naudts and Hodgins, 2006). This pattern is more commonly observed among persons with APD only, associated with defects of behavioral inhibition, attention and other lower-order executive functions (e.g. Damasio, 2000; Vollm et al., 2004). Violent psychotic persons with low psychopathy scores usually present difficulties with higher-order executive functions (e.g. WCST, Tower of London) and lower frontal activation, especially in the superior frontal gyrus, compared with persons with an APD only or non-violent persons with Sz only (Barkataki et al., 2005; Kumari et al., 2006). Thus, it seems that among violent persons with Sz, those with APD and/or SUD constitute a highly different subgroup, in which cognitive, neurological and behavioral patterns are more closely associated with the personality traits than schizophrenia (Hodgins et al., 2005; Krakowski, 2005).

References


