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Cortex and amygdala morphology in psychopathy

Marina Boccardi [a], Giovanni B. Frisoni [a,*], Robert D. Hare [c], Enrica Cavedo [a,b], Pablo Najt [d], Michela Pievani [a], Paul E. Rasser [e,f], Mikko P. Laakso [g,h], Hannu J. Aronen [i,j], Eila Repo-Tiihonen [k], Olli Vaurio [k], Paul M. Thompson [l], Jari Tiihonen [k,m,n]

[a] LENITEM Laboratory of Epidemiology, Neuroimaging, & Telemedicine – IRCCS San Giovanni di Dio-FBF, via Pilastroni, 4, 25100, Brescia, Italy
[b] AFaR Associazione Fatebenefratelli per la Ricerca, Rome, Italy
[c] Department of Psychology, University of British Columbia, and Darkstone Research Group, Vancouver, Canada
[d] Laboratory of Biological Psychiatry – IRCCS San Giovanni di Dio-FBF, Brescia, Italy
[e] Schizophrenia Research Institute, Sydney, Australia
[f] Priority Centre for Brain and Mental Health Research University of Newcastle, Newcastle, Australia
[g] Department of Psychiatry, Kuopio University Hospital, Kuopio, Finland
[h] Department of Clinical Radiology, Kuopio University Hospital, Kuopio, Finland
[i] Department of Radiology, University of Turku, Finland
[j] Department of Radiology, Turku University Central Hospital, Turku, Finland
[k] Department of Forensic Psychiatry, University of Kuopio and Niuvanniemi Hospital, Kuopio, Finland
[l] Laboratory of NeuroImaging, Brain Mapping Division, Department of Neurology, UCLA School of Medicine, Los Angeles, CA, USA
[m] Department of Clinical Physiology, Kuopio University Hospital, Kuopio, Finland
[n] National Institute for Health and Welfare, Helsinki, Finland

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ABSTRACT

Psychopathy is characterized by abnormal emotional processes, but only recent neuroimaging studies have investigated its cerebral correlates. The study aim was to map local differences of cortical and amygdalar morphology. Cortical pattern matching and radial distance mapping techniques were used to analyze the magnetic resonance images of 26 violent male offenders (age: 32±8) with psychopathy diagnosed using the Psychopathy Checklist-Revised (PCL-R) and no schizophrenia spectrum disorders, and in matched controls (age: 35± sp="0.12"/>11). The cortex displayed up to 20% reduction in the orbitofrontal and midline structures (corrected $p<0.001$ bilaterally). Up to 30% tissue reduction in the basolateral nucleus, and 10–30% enlargement effects in the central and lateral nuclei indicated abnormal structure of the amygdala (corrected $p=0.05$ on the right; and symmetrical pattern on the left). Psychopathy features specific morphology of the main cerebral structures involved in cognitive and emotional processing, consistent with clinical and functional data, and with a hypothesis of an alternative evolutionary brain development.

1. Introduction

Psychopathy is a personality disorder defined by interpersonal, affective, lifestyle, and antisocial traits and behaviors, including grandiosity, egocentricity, deceptiveness, shallow emotions, lack of empathy, guilt, or remorse, irresponsibility, impulsivity, and a tendency to violate social norms (Hare, 2003). Psychopathic offenders are responsible for a disproportionate amount of antisocial behaviors, crimes and violence, and are overrepresented in correctional and forensic psychiatric institutions. Psychopathy is conceptually similar to the DSM-IV category of antisocial personality disorder (ASPD). However, the former places more emphasis on interpersonal and affective features, while the latter emphasizes overt antisocial behaviors. A proposal for DSM-V has been formulated (Miller and Holden, 2010), that includes features of psychopathy to be integrated within ASPD personality disorder. The standard tool for the assessment of psychopathy is the Psychopathy Checklist-Revised (PCL-R) (Hare, 2003). Although the PCL-R measures a unitary superordinate construct, confirmatory factor analyses of large data sets support a model in which psychopathy is underpinned by four correlated factors: the *Interpersonal*, *Affective*, *Lifestyle,* and *Antisocial* dimensions (Hare, 2003; Hare and Neumann, 2008).

An extensive literature on autonomic, neurophysiological and functional variables indicates that psychopathy is associated with difficulties in tasks requiring emotional and attentional processing, or the integration of cognitive and emotional information (Hare, 2003; Newman et al., in press). These data indicate that limbic and paralimbic functions of individuals with psychopathy differ from

* Corresponding author at: LENITEM Laboratory of Epidemiology, Neuroimaging, & Telemedicine – IRCCS San Giovanni di Dio-FBF, via Pilastroni, 4, 25100, Brescia, Italy. Tel.: +39 030 3501361; fax: +39 02 700435727.
E-mail address: papers@centroalzheimer.it (G.B. Frisoni).

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those of normal subjects (Veit et al., 2002; Birbaumer et al., 2005; Kiehl, 2006), and support the hypothesis of a possible morphologic involvement of the limbic–paralimbic circuitry (Kiehl, 2006; Blair, 2007). Investigations of the cortical morphology of psychopathy or ASPD do find alterations in the orbitofrontal, ventromedial, cingulate and temporal paralimbic cortices, with some additional but less replicated regions of tissue reductions in the superior temporal gyrus, sulcus, and right dorsal cortices (Table S1). However, only one study (Yang et al., 2009a) used both the PCL-R for the selection of subjects, and the cortical pattern matching (CPM) pipeline (Thompson et al., 2004a), a technique allowing for maximum accuracy in the local mapping of cortical differences. Regarding the amygdala, a recent study found smaller global volumes in individuals with psychopathy (Yang et al., 2009b). Nonetheless, the amygdala tracings were made by two different raters, which may present a major source of inconsistency (Yang et al., 2009b). Moreover, although both studies by Yang et al. (Yang et al., 2009a,b) assessed patients with the PCL-R, the exclusion of or correction for other psychiatric disorders, including those of the schizophrenia spectrum, reported in the original sample (Raine et al., 2000), is not mentioned in these two articles (Table S1).

In the present study we assessed brain morphology in a PCL-R psychopathy sample that was free of schizophrenia spectrum disorders. Larger white matter volumes were found in the parietal, occipital, and left cerebellar lobes of this sample with voxel-based morphometry (VBM) analysis, and lesser gray matter volumes were detected in parietal and paralimbic structures (Tiihonen et al., 2008). Here, we used two magnetic resonance imaging techniques, CPM (Thompson et al., 2004a) and the radial distance mapping (RDM) techniques (Thompson et al., 2004b), that allow more accurate mapping of the cerebral cortex and amygdala than allowed by VBM (Tiihonen et al., 2008). In fact, the first normalizes the brain, taking into account 40 manually traced sulci (Thompson et al., 2004a), and the second reconstructs the 3D shape of convex structures, from their coronal manual tracing (Thompson et al., 2004b). Spatial normalization and manual tracing by a single tracer were carried out for each technique. The a priori hypothesis was that structural differences would have been observed in the amygdala and in the most closely connected structures, belonging to the paralimbic network.

2. Methods

2.1. Subjects

The 26 offenders and 25 controls examined in this study (Table 1), already described in previous studies (Tiihonen et al., 2008; Boccardi et al., 2010) were all Caucasian Finnish men. Offenders were charged with violent offences (2 murders, 10 manslaughters, 4 attempted murders or manslaughters, 1 assisting manslaughter, 6 assaults, and 3 armed robberies), had a history of recurrent violent acts and, with the exception of two cases, had previous convictions for violence. Cases fulfilled the criteria for both DSM-IV ASPD and ICD-10 dissocial personality and for substance abuse (Tiihonen et al., 2008; Boccardi et al., 2010). They had additional personality diagnoses, besides ASPD and substance abuse, but had no history nor current diagnosis of psychosis or schizotypal personality disorder. The PCL-R ratings used to assess psychopathy were made by an experienced psychiatrist, a certified PCL-R user, based on extensive case records (Hare, 2003). The intraclass correlation coefficients were $r = 0.94$ for the PCL-R total score, $r = 0.78$ for Hare's Factor 1, and $r = 0.92$ for Hare's Factor 2. PCL-R ratings were made by a rater blind to the magnetic resonance imaging (MRI) data.

Twenty-five age- and sex-matched healthy volunteers were recruited among students, hospital staff and skilled workers. They were free of current or past substance abuse and mental disorders on the basis of an unstructured interview. They provided informed consent. Data from offenders (MRI scans and case record files) were obtained retrospectively from hospital files, after approval by the local Finnish ethical committee.

Table 1
Sociodemographic and clinical features of the healthy men and the violent offenders.

	Controls ($N = 25$)	Violent offenders ($N = 26$)	P value
Sex (M, %)	25 (100%)	26 (100%)	1.00
Age, years	34.6 ± 10.8	32.5 ± 8.4	0.438
Alcohol dependence, %	0	100%	–
Age onset of alcohol abuse	–	13.6 ± 2.9	–
Polysubstance abuse, %	0	77%	–
Total intracranial volume (cm^3)	1707 ± 117	1654 ± 108	0.102
Hare's Factor 1 (Interpersonal)	–	3.8 ± 2.5	–
Hare's Factor 2 (Affective)	–	6.9 ± 1.2	–
Hare's Factor 3 (Lifestyle)	–	9.7 ± 0.8	–
Hare's Factor 4 (Antisocial)	–	8.5 ± 1.8	–
IQ	–	91.5 ± 9.0	–

Values denote mean ± S.D. P values refer to Student's t and Fisher's exact tests.
The IQ of the offenders was assessed using the Wechsler Adult Intelligence Scale – Revised (Wechsler, 1981).

2.2. Magnetic resonance imaging

The MR images were obtained with a 1.0 T Impact scanner (Siemens; Erlangen, Germany) using a standard head coil and a tilted T1-weighted coronal 3D gradient echo sequence (magnetization prepared rapid acquisition gradient echo: TR of 10 ms, TE of 4 ms, TI of 250 ms, flip angle of 12°, FOV of 250 mm, matrix of 256 × 192, and 1 acquisition). The three-dimensional spatial resolution was 2.0 mm × 1.3 mm × 0.97 mm.

The CPM (Thompson et al., 2004a) and the RDM (Thompson et al., 2004b) techniques were used to study gray matter density (GMD) over the whole cortical mantle and the morphology of the amygdala, respectively.

The 3D images were re-sampled to an isotropic voxel of 1 mm, reoriented along the anterior commissure-posterior commissure (AC-PC) line; voxels below the cerebellum were removed. The anterior commissure was manually set as the origin of the spatial coordinates for an anatomical normalization algorithm implemented as part of the Statistical Parametric Mapping (SPM2) software package (http://www.fil.ion.ucl.ac.uk/spm/software/spm2/). A 12-parameter affine transformation was used for the spatial normalization of each image to a customized template in stereotaxic space, created from the MRI scans of all study subjects.

2.3. Cortical pattern matching (CPM)

Individual brain masks for each hemisphere were extracted. The masks were visually inspected, manually corrected with DISPLAY, and applied to normalized images to obtain 'skull-stripped' images of each hemisphere. A 3D model of the cortical hemisphere surfaces was automatically extracted using intensity information. Normalized images were segmented into gray matter, white matter and cerebrospinal fluid using an algorithm that employs partial volume and bias field correction (Shattuck et al., 2001).

Sulcal lines were traced by a single tracer (PN), blind to diagnosis, on the cortical surfaces according to a previously validated anatomical delineation protocol, after the standard learning procedure. The traced sulci were flattened and averaged across subjects to create a population-specific template based on all the subjects in the study (Thompson et al., 2000). Averaged sulci were then used as landmarks to warp each subject's anatomy onto the template. The same deformation was applied to the segmented images, thus allowing