Atypical nucleus accumbens morphology in psychopathy: Another limbic piece in the puzzle

Marina Boccardi [a,b], Martina Bocchetta [b], Hannu J. Aronen [c,d], Eila Repo-Tiihonen [e], Olli Vaurio [e], Paul M. Thompson [f], Jari Tiihonen [e,g,h,*], Giovanni B. Frisoni [a,**]

[a] LENITEM Laboratory of Epidemiology, Neuroimaging, & Telemedicine - IRCCS San Giovanni di Dio-FBF, Brescia, Italy
[b] AFaR (Associazione Fatebenefratelli per la Ricerca), Rome, Italy
[c] Department of Radiology, University of Turku, Finland
[d] Department of Radiology, Turku University Central Hospital, Turku, Finland
[e] Department of Forensic Psychiatry, University of Eastern Finland and Niuvanniemi Hospital, Kuopio, Finland
[f] Laboratory of NeuroImaging, Department of Neurology & Psychiatry, UCLA School of Medicine, Los Angeles, CA, USA
[g] Karolinska Institutet, Department of Clinical Neuroscience, Stockholm, Sweden
[h] National Institute for Health and Welfare, Helsinki, Finland

ARTICLE INFO

ABSTRACT

Psychopathy has been associated with increased putamen and striatum volumes. The nucleus accumbens – a key structure in reversal learning, less effective in psychopathy – has not yet received specific attention. Moreover, basal ganglia morphology has never been explored. We examined the morphology of the caudate, putamen and accumbens, manually segmented from magnetic resonance images of 26 offenders (age: 32.5 ± 8.4) with medium-high psychopathy (mean PCL-R $= 30 \pm 5$) and 25 healthy controls (age: 34.6 ± 10.8). Local differences were statistically modeled using a surface-based radial distance mapping method ($p < 0.05$; multiple comparisons correction through permutation tests). In psychopathy, the caudate and putamen had normal global volume, but different morphology, significant after correction for multiple comparisons, for the right dorsal putamen (permutation test: $p = 0.02$). The volume of the nucleus accumbens was 13% smaller in psychopathy (p corrected for multiple comparisons < 0.006). The atypical morphology consisted of predominant anterior hypotrophy bilaterally (10–30%). Caudate and putamen local morphology displayed negative correlation with the lifestyle factor of the PCL-R (permutation test: $p = 0.05$ and 0.03). From these data, psychopathy appears to be associated with an atypical striatal morphology, with highly significant global and local differences of the accumbens. This is consistent with the clinical syndrome and with theories of limbic involvement.

© 2013 Elsevier Ltd. All rights reserved.

1. Introduction

Psychopathy is a personality disorder characterized by shallow affect, a callous lack of empathy or remorse, and an inclination to a parasitic and impulsive lifestyle, often leading to criminal behavior (Hare & Neumann, 2008).

Recent research on brain morphology has detected morphological differences in the brain structures of individuals with psychopathy, although differences in the methods used have led to inconsistent results (Koenigs, Baskin-Sommers, Zeier, & Newman, 2010). Differences have been reported in cortical and subcortical regions (Boccardi et al.,

2011; de Oliveira-Souza et al., 2008; Muller et al., 2008; Tiihonen et al., 2008; Yang, Raine, Colletti, Toga, & Narr, 2009). Among these, the basal ganglia are crucial for emotional processing and behavioral planning, particularly via their connections with the amygdala and the frontal lobe, within the limbic circuit (Devinsky, Morrell, & Vogt, 1995; Vogt, Finch, & Olson, 1992). Indeed, the hypothesis that psychopathic behavior may correlate with differences in the limbic structures and connections has been repeatedly corroborated (Craig et al., 2009; Kiehl, 2006; Raine, Lee, Yang, & Colletti, 2010).

Some morphometric studies have found striatal volume alterations in conditions associated with violent behavior. One study found greater global volumes of the putamen in a group of subjects with antisocial personality disorder (ASPD) subjects (Barkataki, Kumari, Das, Taylor, & Sharma, 2006), which was interpreted as possibly related to impulsivity and poor behavioral control. A second study (Glenn, Raine, Yaralian, & Yang, 2010) examined the volume of the entire striatum, of the nucleus lenticularis (putamen and pallidus), and of the caudate head and body, in psychopathy. It found a 9.6% increase for the whole striatum, and

similar enlargement of the nucleus lenticularis, bilaterally; findings were interpreted as connected to the increased stimulation seeking and impairments in reinforcement learning in psychopathy. A recent voxel-based morphometry (VBM) study detected greater local gray matter volume in the right caudate and in the left accumbens nuclei in offenders with sub-threshold psychopathy scores (Schiffer et al., 2011).

Nonetheless, only global volumes, or local gray matter density in voxel-based analyses, were examined, and information on the actual 3D shape of the basal ganglia is lacking to date. Moreover, the previous studies did not carry out specific region-of-interest analyses for the nucleus accumbens, the critical basal ganglia nucleus connecting to the amygdala and the orbitofrontal cortex within the anterior limbic circuit (Devinsky et al., 1995; Vogt et al., 1992), which is known to be involved in psychopathy (Boccardi et al., 2011; de Oliveira-Souza et al., 2008; Kiehl, 2006; Raine et al., 2010; Yang, Raine, Narr, Colletti, & Toga, 2009). The accumbens is a key structure in *reversal learning*, i.e., the ability to overwrite on previously learned knowledge as context conditions change. Particularly, individuals need to take experience into account, and update the values that they attributed to stimuli or goals, as well as knowledge about the effects of their own behavior. A goal, or a behavior, that turned out to be good value in the past may not be worth or useful in a different time or context, so the individual must overwrite on prior knowledge in order to engage in more adaptive actions. Considering the limited ability of people with psychopathy to learn from experience, and that many are refractory to different kinds of treatment or correctional contexts, the accumbens is a particularly interesting target for neuroscientific investigation, to assess the neurobiological correlates of the cognitive and volitional capacities generating behavior in psychopathy.

Here we aimed to quantify the global volume of the caudate, putamen and accumbens nuclei, and to map local morphological differences using the radial distance mapping algorithm. We examined a sample of criminal offenders with psychopathy as defined by the Psychopathy Checklist Revised (PCL-R), lacking disorders in the schizophrenia spectrum, which are associated with independent brain alterations in individuals with violent behavior (Narayan et al., 2007).

2. Materials and methods

2.1. Subjects

Study subjects with psychopathy, already described in detail (Boccardi et al., 2010, 2011; Tiihonen et al., 2008), included 26 habitually violent male offenders, consecutively admitted to a university forensic psychiatric hospital for pre-trial assessment, and currently charged with a violent offence. They fulfilled criteria for DSM-IV ASPD and ICD-10 dissocial personality, had no history or current diagnosis of psychosis or schizotypal personality disorder, had additional cluster B personality disorders and met criteria for substance abuse.

The PCL-R was used to assess psychopathy (Hare, 2003) by a certified psychiatrist.

Twenty-five healthy men volunteers of similar age, free from current or past substance abuse, were recruited among students, hospital staff and skilled workers, after giving informed consent (Boccardi et al., 2010; Tiihonen et al., 2008). The magnetic resonance imaging (MRI) scans and case record files of the offenders were obtained retrospectively from hospital files, after approval by the ethics committee of the Kuopio University Hospital.

2.2. Magnetic Resonance Imaging

MRIs were acquired on 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 10 ms, TE 4 ms, TI 250 ms, flip angle 12°, FOV 250 mm, matrix 256×192, 1 acquisition). The three-dimensional spatial resolution was 2.0 mm×1.3 mm×0.97 mm.

2.3. Image processing

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

2.4. Manual segmentation

The putamen, caudate and accumbens of offenders and controls were manually traced by a single tracer (Martina Bocchetta), blind to diagnosis, following an optimized protocol based on the selection of landmarks and criteria from three validated protocols (Gunning-Dixon, Head, McQuain, Acker, & Raz, 1998; Hokama et al., 1995; Makris et al., 1999). Criteria were chosen if they: 1) included more of the selected region of interest (ROI), 2) were better defined, or 3) were the most often used. Intra-class correlation coefficients (ICC) were previously obtained on an independent sample of 10 controls from a local dataset (Galluzzi et al., 2009), scanned with a machine of the same magnet strength as that used for the sample of psychopathic and healthy subjects examined here. The intra-rater reliability measures were 0.92 for the accumbens and caudate, 0.98 for the putamen; the reference for the computation of inter-rater reliability consisted in the segmentation of the basal ganglia of the same subjects by another tracer, expert of cerebral anatomy (Enrica Cavedo). Inter-rater measures were 0.83 for the accumbens, 0.89 for the putamen and 0.91 for the caudate.

2.4.1. Criteria for manual segmentation of the nucleus accumbens, caudate nucleus and putamen from magnetic resonance images

Tracing proceeds on contiguous coronal brain sections from caudal to rostral. For a slice thickness of 1 mm, approximately 15 slices include the accumbens, 60 the caudatus, and 50 the putamen.

2.4.1.1. Accumbens.
Tracing starts (Fig. 1j) on the section rostral to the slice where the anterior commissure decussates (Fig. 1i), and stops (Fig. 1k) when the putamen is no longer visible in the coronal section, as confirmed by the axial view. The separation of the accumbens from the putamen and the caudate is helped by the tracing of two arbitrary lines. A horizontal line tangent the inferiormost tip of the lateral ventricle distinguishes any superior gray matter, characterized by a lighter gray than the accumbens, as belonging to the caudate (yellow line in the Fig. 1j–k); a vertical line drawn from the most inferior point of the internal capsule, upwards to the caudatus, discriminates any lateral gray matter as belonging to the ventral putamen (green line in the Figure, j–k) (Makris et al., 1999).

2.4.1.2. Caudate.
The tracing of the caudate includes the head, the body, and the tail, as long as it is adjacent to the lateral ventricle, and excludes the caudal portion curving in the anteroventral direction (Hokama et al., 1995). The tracing starts on the most caudal slice (Fig. 1c) on which the tail is adjacent to the lateral ventricle, as also visible on the axial plane (Fig. 1a). The head is traced until it is no longer visible, on the most rostral section on which the nucleus is usually adjacent to the lateral ventricle (Fig. 1l), as confirmed on the axial view (Fig. 1m). The caudate is bordered medially by the lateral ventricle, laterally by the internal capsule and dorsally by lobar white matter (Fig. 1c–l).