CORTEX 49 (2013) 2178–2185

Available online at www.sciencedirect.com

SciVerse ScienceDirect

Journal homepage: www.elsevier.com/locate/cortex

Research report

# Reduced thickness of anterior cingulate cortex in obsessive-compulsive disorder

Simone Kühn [a,b,c,*], Christian Kaufmann [d], Daniela Simon [d], Tanja Endrass [d], Jürgen Gallinat [b] and Norbert Kathmann [d]

[a] Ghent University, Faculty of Psychology and Educational Sciences, Department of Experimental Psychology, Ghent Institute for Functional and Metabolic Imaging, Gent, Belgium
[b] Charité University Medicine, St Hedwig Krankenhaus, Clinic for Psychiatry and Psychotherapy, Berlin, Germany
[c] Physikalisch-Technische Bundesanstalt (PTB), Berlin, Germany
[d] Department of Psychology, Humboldt-Universität zu Berlin, Berlin, Germany

ARTICLE INFO

*Article history:*
Received 29 September 2011
Reviewed 10 November 2011
Revised 22 April 2012
Accepted 5 September 2012
Action editor Jordan Grafman
Published online 17 September 2012

*Keywords:*
Obsessive-compulsive disorder
Cortical thickness
Anterior cingulate cortex
Symptom severity
FreeSurfer

ABSTRACT

*Introduction:* Obsessive-compulsive disorder (OCD) is characterized by a pattern of repetitive, intrusive thoughts and behaviours that patients do not want to but feel they have to perform. Functional brain imaging revealed dysfunctional pathways in OCD involving the anterior cingulate cortex (ACC), orbitofrontal cortex (OFC), and basal ganglia. Structural alterations in OCD have been discussed but analysis tools focussing on specific morphometric aspects such as cortical thickness have rarely been employed.
*Methods:* We acquired MRI scans from 101 OCD patients and 95 healthy control subjects. FreeSurfer analysis software was employed to model the individual grey–white and pial surfaces to compute cortical thickness as our target measure.
*Results:* Relative to controls, OCD patients demonstrate cortical thinning in dorsal and subgenual ACC (false discovery rate corrected at $p < .001$), as well as in several other regions within the fronto-parietal network (false discovery rate corrected at $p < .05$). Cortical thickness could not be predicted in whole brain analyses from symptom state, but there was a modest correlation of left dorsal ACC thickness with the obsession subscore of the Yale-Brown Obsessive-Compulsive Scale as well as with the Beck Depression Inventory score.
*Conclusions:* The findings confirm and extend previous reports showing that OCD is associated with morphometric alterations. The location of the most robust cortical thinning in ACC regions matches the previously reported topography of functional alterations at resting state and during cognitive task execution.



* *Corresponding author*. Ghent University, Faculty of Psychology and Educational Sciences, Department of Experimental Psychology, Ghent Institute for Functional and Metabolic Imaging, 9000 Gent, Belgium.
E-mail addresses: kuehn@mpib-berlin.mpg.de, simone.kuhn@ugent.be (S. Kühn).
0010-9452/$ – see front matter © 2012 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.cortex.2012.09.001

## 1. Introduction

Obsessive-compulsive disorder (OCD) is a psychiatric disorder which affects about 2–3% of the general population during lifetime and about 50 million people worldwide (Ruscio et al., 2010). OCD has been considered one of the leading causes of disability (Michaud et al., 2006). The disorder affects thoughts (obsessions) as well as actions (compulsions) and emotions. Compulsions consist of repetitive or ritualized behaviours including actions that patients do not *want* to but feel they have to perform, e.g., washing, household safety checking, counting, constant checking of oneself and others to ensure no harm has occurred. Obsessions consist of intrusive and unwanted thoughts and are most often concerned with themes of contamination, order and symmetry of objects, or fear of harming oneself or others. The neural basis of OCD has been explored in functional as well as structural neuroimaging studies. A recent qualitative meta-analysis on volumetric studies in OCD identified reductions in left anterior cingulate cortex (ACC) and bilateral orbitofrontal cortex (OFC) and increases in bilateral thalamus (Rotge et al., 2009). A quantitative meta-analysis including solely studies based on voxel-based morphometry (VBM) found reductions of grey matter density in the fronto-parietal network, including dorsolateral prefrontal cortex, OFC and increases in putamen and inferior frontal gyrus (Rotge et al., 2010). Another meta-analysis following the same rationale found concurrence across studies in bilateral lenticular nuclei (extending to caudatus) increases and ACC and dorsal medial frontal decreases (Radua and Mataix-Cols, 2009).

VBM has been applied to a number of different psychiatric and neurological disorders contributing to the understanding of how the brain changes in these disorders. Although results from VBM studies are generally difficult to validate, studies have compared results of VBM analyses to manual and visual measurements of particular structures and have shown relatively good correspondence between the techniques (Good et al., 2002), providing some confidence in the validity of VBM (Whitwell, 2009). However, a disadvantage of VBM is that it is sensitive to a combination of changes in grey matter thickness, intensity, cortical surface area and cortical folding (Hutton et al., 2009; Voets et al., 2008). VBM is prone to smoothing across neighbouring gyri, whereas the cortical surface approach (FreeSurfer toolbox) used in the present study smoothes on the inflated cortical surface. Moreover, VBM is susceptible to differences in registration and choice of normalization template (Bookstein, 2001; Jones et al., 2005). Therefore, brain surface-based morphology analysis has been put forward to assess the contribution of grey matter thickness – independently of regional surface area (Voets et al., 2008). Cortical thickness has previously been shown to be associated with normal ageing, intelligence, cognitive performance and mental disorders and is suggested as a sensitive parameter with a high signal-to-noise ratio (Choi et al., 2008; Dickerson et al., 2008; Hutton et al., 2009; Salat et al., 2004). Furthermore, cortical thickness measures are more easily interpretable than the probabilistic grey matter volumes in VBM (Lehmann et al., 2009). Therefore, cortical thickness may be considered a more appropriate measure when trying to measure brain structural differences between OCD patients and healthy controls. To our knowledge, only two studies have used cortical thickness to explore structural abnormalities in OCD, with inconsistent findings. Narayan et al. (2008) observed increases of cortical thickness in right inferior frontal cortex and posterior middle temporal gyrus, and decreases in left supramarginal gyrus and pregenual ACC when comparing 21 OCD with 21 control participants. Shin et al. (2007) found cortical thinning in left inferior frontal, middle frontal, precentral, superior temporal, parahippocampal, orbitofrontal and lingual cortices in a larger sample consisting of 55 OCD patients and 52 controls. Neither of these studies reported associations between structural abnormalities and symptom severity. In order to further clarify this issue and to enhance reliability of findings we analyse the anatomical images of 101 OCD patients and 95 control subjects. In addition, we relate cortical thickness within regions of significant difference to clinical symptom measures.

## 2. Methods

### 2.1. Participants

196 subjects, with 101 (52 females, 49 males) of them having a diagnosis of OCD-, and 95 (52 females, 43 males) control subjects without any diagnosis of mental disorder participated in this study. Patients were recruited from an outpatient clinic specialized in the treatment of OCD located at the Department of Psychology, Humboldt-University at Berlin, Germany. Patients were consecutively enrolled from clinic admissions if they agreed to participate and fulfilled inclusion criteria. Controls were recruited by means of newspaper advertisements. Patients qualified as participants if they were assigned a primary diagnosis of OCD after having conducted the Structured Clinical Interview for diagnostic and statistical manual of mental disorders (DMS-IV) (SCID, First et al., 1995) by trained clinical psychologists, and if they had an age between 18 and 60 years. Exclusion criteria for the OCD patient group were an additional past or present diagnosis of psychotic disorder or substance dependence. Control participants were included if they were free of any axis I mental disorder for lifetime, as confirmed by a SCID screening interview, and if they had not taken psychotropic medication during the last four weeks. Both patients and control participants were excluded if they showed interfering medical conditions, like neurological disorders. In addition, the common safety criteria for exclusion from magnetic resonance imaging (MRI) scans were applied such as cardiac pacemakers etc. Most patients and controls being analysed in this study also underwent functional MRI scanning (results not reported here). Forty (40%) patients were medicated at the time of scanning or during the past week, mostly with serotonin reuptake inhibitors (SSRI). Specifically, nine patients received citalopram, eight fluoxetine, seven paroxetine, five escitalopram, three clomipramine, three venlafaxine, and two sertraline. In addition, quetiapine, risperidone, and promethazine were administered in one patient each. Present or past comorbid axis I mental disorders were diagnosed in 54 (55%) OCD patients. Comorbid diagnoses