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Fluvoxamine Treatment and D_2 Receptors: a Pet Study on OCD Drug-Naïve Patients

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Changes in D_2 receptors during antidepressant therapy have been reported in patients with major depressive disorder using PET/SPET. The aim of this study was to evaluate modifications in D_2 receptors that might occur in patients affected by obsessive-compulsive disorder (OCD) during serotonin reuptake sites inhibitors (SSRIs). To this purpose, we measured the *in vivo* binding of [^{11}C]raclopride ([^{11}C]Rac)in the brain of a group of OCD naïve patients before and after the repeated administration of the inhibitor SSRI fluvoxamine. Eight patients with a Diagnostic and Statistical Manual of Mental Disorders IVth edition diagnosis of OCD completed the study undergoing a PET scan and a complete clinical evaluation before and during treatment with fluvoxamine. Patients have been compared also with a group of nine age-matched normal volunteers. Fluvoxamine treatment significantly improved clinical symptoms and increased [^{11}C]Rac binding potential (BP) in the basal ganglia of OCD patients (7.5 ± 5.2, 6.9 ± 6.9, and 9.9 ± 9.3% in dorsal caudate, dorsal putamen, and ventral basal ganglia, respectively; $p < 0.01$) to values closer to those observed in the group of normal subjects. Chronic treatment with fluvoxamine induces a slight but significant increase in striatal [^{11}C]Rac BP of previously drug-naïve OCD patients. The modifications in D_2 receptor availability might be secondary to fluvoxamine effects on serotoninergic activity.
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INTRODUCTION

Obsessive-compulsive disorder (OCD) is a heterogeneous mental disorder, often disabling, with different clinical presentations, including primary obsessions and secondary (obsession-dependent) compulsions. Several theories indicate that OCD has biological as well as psychological causes. Although the molecular causes of OCD remain unsolved, a dysfunction in a neuronal loop running from the orbital frontal cortex to the cingulate gyrus, striatum (caudate nucleus and putamen), globus pallidus, thalamus, and back to the frontal cortex has been suggested. This hypothesis is supported by neurological (Laplane *et al*, 1989), neurosurgical (Mindus *et al*, 1994; Oliver *et al*, 2003; Rauch, 2003), and imaging findings (Baxter *et al*, 1992; Breiter *et al*, 1996; Saxena *et al*, 1998; Trivedi, 1996). The exact nature of the molecular events that evoke OCD symptoms is not known and several hypotheses have been put forward. The activity of 'OCD loop' is regulated by different neurotransmitters including: glutamate, serotonin dopamine, and GABA (McDougle *et al*, 1993). In particular, cortical glutamatergic neurons present within the circuit co-express dopamine D_1 and serotonin $5HT_2$ receptors, whereas dopamine D_2 receptors are expressed by cortical presynaptic inhibitory interneurons and postsynaptic striatal neurons. The clinical efficacy of serotonin reuptake sites inhibitor (SSRI) has focused the role of serotonin and serotonin receptors in OCD (Baumgarten and Grozdanovic, 1998). However, other findings suggest a possible role also for dopamine and dopamine receptors. In particular, (a) dopamine regulates cortico-striatal-thalamo-cortical circuits through its activity on indirect and direct pathway (Alexander and Crutcher, 1990); (b) structural damages to the basal ganglia, a region particularly rich in dopamine receptors, promote OCD symptoms (Carmin *et al*, 2002); (c) a supersensitivity to cataleptic induction by the D_2 receptor antagonist sulpiride was observed in the D1CT mice, an animal model that shows symptoms of human compulsive disorders associated with cortical-limbic hyperactivity (Campbell *et al*, 1999); (d) differences in D_2 dopamine receptor binding in the head of the caudate nucleus predict phenotypic severity in

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monozygotic twins discordant for Tourette syndrome severity (Wolf *et al*, 1996); and (e) a reduced availability of D_2 receptors subtypes has been recently described in the left caudate nucleus of patients with OCD (Denys *et al*, 2004). In addition, preclinical studies on rodents indicated that the repeated administration of antidepressants affect dopamine D_2 receptors (Ainsworth *et al*, 1998a; Ainsworth *et al*, 1998b; Spyraki and Fibiger, 1981). A modulation of dopaminergic system after SSRIs administration has also been demonstrated *in vivo* using imaging techniques. In particular, serotoninergic neurons have been found to tonically inhibit the nigrostriatal dopamine system, an effect that is probably modulated via 5HT2A receptors (Dewey *et al*, 1995). A modification in D_2 receptors availability has been observed in patients suffering from major depression treated with SSRI. An increased D_2 receptor availability has been demonstrated in the striatum and anterior cingulate gyrus of unipolar depressed patients responders to SSRI treatment but not in nonresponder patients (Klimke *et al*, 1999; Larisch *et al*, 1997).

Up to now, no one has attempted to investigate *in vivo* in OCD patients the effect of SSRI treatment on dopamine D_2 receptors. The aim of this study was to assess the effect of repeated administration of the selective SSRIs fluvoxamine on the *in vivo* binding of [^{11}C]raclopride ([^{11}C]Rac), a selective D_2 dopamine receptor antagonist, in the basal ganglia of patients with OCD. To avoid the effect of any antidepressant therapy performed before the PET study, the *in vivo* binding of [^{11}C]Rac was examined in a group of drug-naïve patients before and after clinical response to fluvoxamine therapy.

PATIENTS AND METHODS

Patients

Nine subjects, six males and three females, with a clinical diagnosis of primary OCD according to the Diagnostic and Statistical Manual of Mental Disorders IVth edition (DSM-IV) criteria, were included in the study. Each subject signed a written informed consent according to the study protocol that was approved by the Ethical Committee of the Scientific Institute H San Raffaele. Patients were recruited in the Psychiatric Department of the Scientific Institute S Raffaele Hospital, Milan. All patients were evaluated by psychiatrists and diagnosed as having OCD, according to the criteria of the DSM-IV (American Psychiatric Association, 1994). Patients were drug naïve for antidepressants, mood stabilizers, such has lithium, anticonvulsants, and neuroleptics. The previous use of benzodiazepines, unless chronic, was not considered an exclusion criterion. Their use was permitted at the time of the study if the clinical conditions of the patients made it necessary, but patients were required to suspend, if possible, the use of benzodiazepines for a period of at least five half-lives of the drug, before PET study. Patients assuming benzodiazepines at the time of first PET examination maintained the drug assumption at the same dosage at the time of second PET study. A complete physical examination was performed at the time of recruitment to exclude any systemic or neurologic disease. A history of birth and head trauma and any other diagnosis of Axis I according to the DSM-IV were considered exclusion criteria. All patients were evaluated by means of structured psychiatric interview (DIS (Robins, 1989)) based on DSM-IV for Axis I diagnoses. Each patient was examined with the Yale–Brown Obsessive Compulsive Scale (Y-BOCS), administered the same day of each PET scan. Patients were considered as fluvoxamine responders when their initial Y-BOCS scores were reduced by at least 35% (Goodman and Price, 1992; Mundo *et al*, 1997). D_2 receptors availability of OCD patients measured before or during fluvoxamine administration were compared with that of a group of nine healthy individuals (one female and eight males) ranging from 22 to 48 years (mean: 26.55 ± 8.32 years).

Pharmacological Treatment and Study Design

The effect of fluvoxamine was evaluated by means of a within-subject trial. Each patient underwent a PET study before (PET-I) and after (PET-II) a minimum of 12 weeks' fluvoxamine full-dose treatment. Each patient started fluvoxamine treatment the night after the PET-I study. Starting dose was 50 mg once a day increased to 50 mg every 4 days to reach the maximum dose of 300 mg/day (range: 150–300 mg/day).

PET Studies

PET studies were performed with an 18-ring tomograph (GE Advance; General Electric Medical System, Milwaukee, WI, USA). One 10-min transmission scan was carried out with an external ^{68}Ge ring source. At the end of the transmission scan, patients received an intravenous injection of 5 ml of saline solution containing approximately 1.07 ± 05 nmol of [^{11}C]Rac (PET-I—mean dose: 218 ± 67 MBq, range: 148–318 MBq, mean specific activity at the time of injection: 50 ± 20 MBq/μmol; PET-II: mean dose: 235 ± 71 MBq, range: 185–66 MBq, mean specific activity at the time of injection: 56 ± 41 MBq/μmol). Immediately after tracer injection, 35 sequential scans (slice thickness 4.25 mm; axial field of view 15.5 cm) were simultaneously acquired in 3D mode, according to the following schedule: four scans of 1 min each followed by three scans of 2 min each and 10 scans of 5 min each (total scanning time = 60 min). Trans-axial images were reconstructed using a Shepp–Logan filter (cutoff 5 mm filter width) in the transaxial plane, and a Shepp–Logan filter (cutoff 8.5 mm) in the axial direction. Images were corrected for decay and attenuation by means of a 10-min transmission scan performed before radioligand injection.

Data Analysis

Reconstructed images derived from normal subjects and patients were transferred to a SUN-SPARC workstation for image processing. Each plane was realigned over time to correct for patient's movement during acquisition time using SPM99 software. [^{11}C]Rac binding to dopamine D_2 receptors was calculated using the simplified reference tissue model (Lammertsma *et al*, 1996). This model allows the calculation of the binding potential (BP) of the radioligand for the receptor of interest (in our case [^{11}C]Rac and dopamine D_2) and the relative influx of

radioactivity (RI) using a brain area devoid of the receptor of interest (in our case the cerebellum), as a reference region. Radioactivity distribution images were transformed pixel by pixel into BP images and relative influx images (RI) using the RPM (reversible reference tissue model) software developed by R Gunn *et al* (Gunn *et al*, 1997). Parametric images were then normalized to the Montreal Neurological Institute (MNI) stereotactic space (Evans *et al*, 1993) using SPM99 software (Wellcome Department of Imaging Neuroscience). Fluvoxamine effect was evaluated using both an automatic localization of significant changes in [^{11}C]Rac binding at a voxel level (SPM99) and a region of interest (ROI) analysis. Both analyses were performed on BP images normalized to an MNI-raclopride template described previously (Meyer *et al*, 1999). ROIs were defined on the standard Montreal Neurological Institute (MNI)-space T1-weighted MRI, corresponding to the MNI-raclopride and positioned according to the method described by Mawlawi *et al* (2001). The following regions were sampled: ventral striatum, bilaterally (VST), dorsal caudate, bilaterally (DCA), and dorsal putamen, bilaterally (DPU).

Statistical analysis in SPM included analysis of t map (SPM(t)) to evaluate differences between conditions (naïve *vs* fluvoxamine treatment), correlations or groups (normal subjets *vs* patients in naïve condition; normal subjets *vs* patients during treatment condition). BP images were masked to include only signal from the basal ganglia, based on $p > 0.5$ (Ashburner and Friston, 1997).

Statistical analysis of ROIs was performed using the Wilcoxon sum-rank test for paired data when comparing clinical scores or BP values assessed within each single region (caudate or putamen) before and during fluvoxamine treatment. Absolute and relative ((PET-I-PET-II)/PET-I) differences for clinical scores and BP values were calculated. As no differences were detected between sides, the condition effect was evaluated on mean regional values. Bonferroni's correction was applied for multiple comparisons. Spearman correlation coefficients were also calculated between pre–post-treatment absolute and relative differences in test scores and [^{11}C]Rac BP.

BP values of OCD patients sampled at PET-I or at PET-II were also compared with those obtained from normal subjects using a Student's t-test for unpaired data. Age was not considered as confounding variable as no significant differences between patients and controls were detected (mean age values: 28 ± 5 and 26 ± 8 years, respectively).

RESULTS

Pharmacological Treatment

Clinical and demographic characteristics of OCD patients are shown in Tables 1 and 2. None of the patients included in the study received benzodiazepine treatment before or during PET studies. Drug response was evaluated by reduction in Y-BOCS total score after 12 weeks of full-dose drug treatment. None of the patients had to interrupt the pharmacological treatment because of side effects but one patient refused to undergo the second PET study. Eight patients (28.7 ± 4.6 years; six males) completed the study performing the second PET scan 4.2 ± 1.5 months later fluvoxamine treatment significantly improved clinical symptoms as revealed by the mean reduction of Y-BOCS total scores (mean relative difference: -43.54%, $p = 0.003$; mean absolute values at PET-I: 29.5 ± 4.7; mean absolute values at PET-II: 17 ± 8.7), compulsions total scores (mean relative difference: -40.92%, $p = 0.002$; mean absolute values at PET-I: 15.2 ± 2.7; mean absolute values at PET-II: 9 ± 3.7), obsessions total scores (mean relative difference: -38.12%, $p = 0.01$; mean absolute values at PET-I: 14 ± 2.6; mean absolute values at PET-II: 9.25 ± 4.6). In three patients, fluvoxamine was not effective: one patient (no. 4) showed totally lack of modifications both in the clinical scales and in the subjective weighted improvement, whereas

Table 1 Clinical Data of Patients

Patient	Other axis I diagnosis	First degree familial psychiatric illnesses	Obsessions	Compulsions	Insight (B–F)[a]
1		Panic attack OCD Tic	Contamination Somatic Others	Wash Check	3–2
2			Aggressive Magic thought	Check Repetitive rituals	1–1
3		OCD	Aggressive Sexual Religious	Repetitive rituals Mental rituals	1–1
4			Contamination Order Somatic Others	Wash Check Ordering Others	2–2
5	Compulsive buying	OCD Major depression	Aggressive Magic thought Order	Check Mental rituals Magic rituals	1–1
6			Order	Ordering	1–1
7			Contamination	Wash	3–3
8			Contamination	Wash	2–1

[a]B–F = Insight dimension before (B) and during fluvoxamine (F).

Table 2 Demographic and Clinical Data of Patients

Patient	Gender	Age (years)	Onset (years)	Y-BOCS	OBS	COMP	CGI	NIMH
1	F	27	5	32	15	17	5	12
2	M	31	20	27	14	13	5	10
3	M	25	12	30	15	15	4	11
4	M	20	4	35	19	16	6	12
5	F	31	8	22	11	11	4	10
6	M	29	23	36	16	20	5	13
7	M	33	14	28	14	14	5	10
8	M	34	20	26	11	15	4	10
Mean		28±5	3±7	29±5	14±3	15±3	4.7±0.7	11±1

M, male; F, female; Y-BOCS, Yale–Brown Obsessive-Compulsive Scale total scores; OBS, Y-BOCS Obsessions scores; COMP, Y-BOCS Compulsion scores; CGI, Clinical global impression scores; NIMH, National Institute of Mental Health Obsessive-Compulsive Scale.
Data are representative of the mean±SD and each single values of fluvoxamine dose, treatment duration, and the percentage of variation of clinical scores.

Table 3 Pharmacological Data of Patients who Completed the Study

Patient	Fluvo (mg/day)	Treatment (months)	Y-BOCS (% mod.)	OBS (% mod.)	COMP (% mod.)	CGI (% mod.)	NIMH (% mod.)
1	200	3	−68.7	−33.3	−41.2	−60	−50
2	300	6	−25.9	−28.6	−23.1	−40	−20
3	200	5	−33.3	−33.3	−33.3	−25	−36.4
4	300	3	0	0	0	0	0
5	200	7	−72.7	−72.7	−72.7	−50	−40
6	150	3	−55.6	−50	−60	−60	−46.1
7	250	3	−57.1	−57.1	−57.1	−60	−40
8	250	4	−35	−30	−40	−25	−30
Mean	233±50	4.2±1.5	−43.5±24.5	−38.1±21.9	−40.9±22.9	−40.0±21.9	−32.8±16.2

Y-BOCS, Yale–Brown Obsessive-Compulsive Scale total scores; OBS, Y-BOCS Obsessions scores; COMP, Y-BOCS Compulsion scores.
Data are representative of the mean±SD and each single values of: Fluvoxamine dose, treatment duration, and the percentage of variation of clinical scores.

the other two (nos. 2 and 3) experienced some symptoms improvement but not enough to classify them as clinical responders (Table 3).

D_2 Receptors Binding

Statistical analysis, based on Wilcoxon test, shows that chronic treatment with fluvoxamine increased the *in vivo* binding of [^{11}C]Rac in the basal ganglia of previously drug-naïve OCD patients. Mean BP values measured before and after fluvoxamine treatment, and the uncorrected *p*-values are shown in Table 4. After clinical response, fluvoxamine significantly increased [^{11}C]Rac BP values in all basal ganglia subregions. In the cerebellum, we failed to find any significant differences in the mean values of integrated radioactivity concentration divided by the injected doses between pre- and post-treatment condition (naïve: 0.0021 ± 0.0017; fluvoxamine: 0.0018 ± 0.0006; $p=0.810$) indicating that the increase in [^{11}C]Rac BP found after fluvoxamine was not due to changes in radioactivity concentration in the reference region. No significant condition differences were found between tracer-specific activity and injected dose. Single subjects modifications of [^{11}C]BP in VST, DCA, and DPU are shown in Figure 1. After treatment with fluvoxamine, symptoms significantly or partial remittance and increase of [^{11}C]Rac BP were consistently found in seven out of the eight subjects examined (VST: range: 2.36–22.16%; DCA: range: 0.45–14.50%; DPU: range: 2.06–17.32%). In the remaining subject

Table 4 Mean Values of Rac BP (Absolute Values and Percentage Changes) Before and After Treatment with Fluvoxamine

Region	BP-PET-I	BP-PET-II	% Changes	*p**
DCA	2.04±0.19	2.18±0.12	+7.9	0.0078
DPU	2.41±0.2	2.56±0.13	+6.9	0.015
VST	1.56±0.11	1.71±0.07	+9.7	0.0078

DCU, dorsal caudate; DPU, dorsal putamen; VTS, ventral striatum.
Values are the mean±SD of [^{11}C]Rac BP of the eight patients who underwent two PET scans.
*Wilcoxon *t*-test for paired comparison.

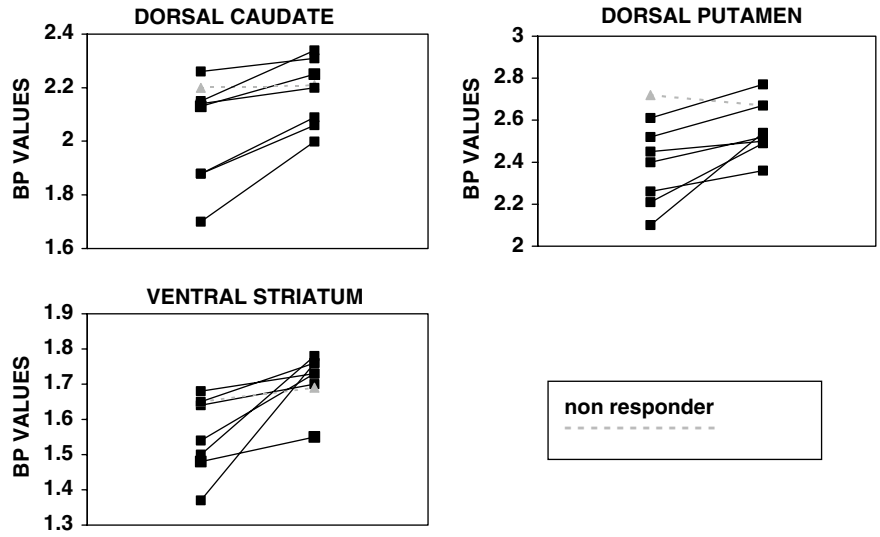

Figure 1 Modifications in individual BP values in the DCA, DPU, and VST of each of the eight patients who completed the study measured before (PRE) and during fluvoxamine therapy. Modifications of BP values of subject 4, the only patient who did not respond at the time of the second PET scan, are indicated as dotted line.

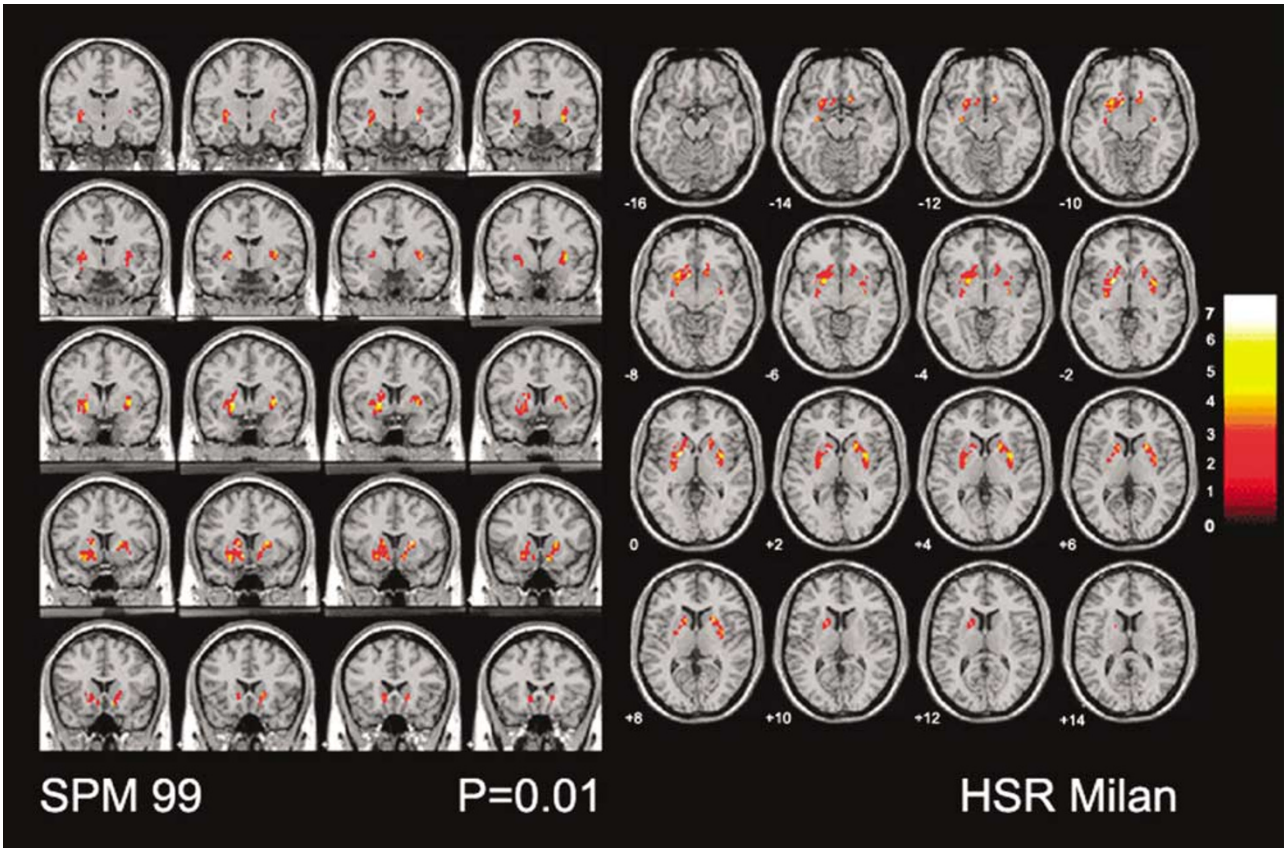

Figure 2 SPM99 analysis. Axial and coronal view of the clusters of significant differences in [^{11}C]Rac BP between naïve and fluvoxamine conditions (paired *t*-test, *p* threshold = 0.01). As indicated by the figure, repeated administration of fluvoxamine induced a mean increase of D_2 receptors availability.

(no. 4), the increase in BP was present in VST but not in DCA and DPU where a slight decrease was observed. Interestingly, in the same subject we failed to observe any reduction in the clinical scale scores. However, using Spearman coefficient analysis we did not found any significant correlation between (a) illness duration, age of onset, clinical score, and BP values measured during naïve condition and (b) modifications in clinical scores and BP values induced by fluvoxamine treatment.

A significant increase in receptors availability was also observed using the voxel-based analysis SPM99. Clusters of significant increase in BP values were observed in the left

($Z = 3.63$) and right ($Z = 3.44$) putamen and in the left ($Z = 3.60$) and right caudate ($Z = 3.59$) (Figure 2).

In naïve conditions, striatal [^{11}C]Rac BP were significantly lower than those observed in normal subjects (Perani *et al*, 2006). However, after fluvoxamine treatment, the mean values of BP were closer to those observed in normal subjects and particularly in the DCA where no significant differences between groups were observed (Table 5). Similar results were obtained using SPM. As showed in Figure 3, after fluvoxamine treatment, regional differences between patients and normal subjects were confined to the left aspects of VST (p threshold = 0.01).

Table 5 Mean Values of Rac BP in the Group of Normal Subjects and Relative Differences with the Group of OCD Patient Evaluated at PET-I or at PET-II

Region	BP-normal	% PET-I	% PET-II
DCA		−10.1*	−4.1
DPU			−4.3*
VST		−15.7**	−7.6*

Values are the mean ± SD of [^{11}C]Rac BP of the nine normal subjects. Mean values of the mean relative differences between OCD patients evaluated at PET-I or PET-II and normal subjects are also reported.
*$p < 0.05$; **$p < 0.001$. Student's t-test between normal subjects and OCD patients evaluated at PET-I and normal subjects and OCD patients evaluated at PET-II.

DISCUSSION

The aim of our study was to evaluate whether SSRI treatment was able to modify dopaminergic system and in particular dopamine D_2 receptors availability in OCD patients. To start the evaluation of this issue and in order to avoid confounding results deriving from previous pharmacological treatments, the study was conducted on a small group of subject never treated with SSRI or other medications used in OCD patients. However, despite the small number of subjects our sample has the clear advantage to present regional values of D_2 receptors availability completely independent from the residual effects of previous pharmacological therapies.

Repeated administration of fluvoxamine significantly modifies striatal D_2 receptors availability. In particular, an increase in [^{11}C]Rac BP was consistently found in all

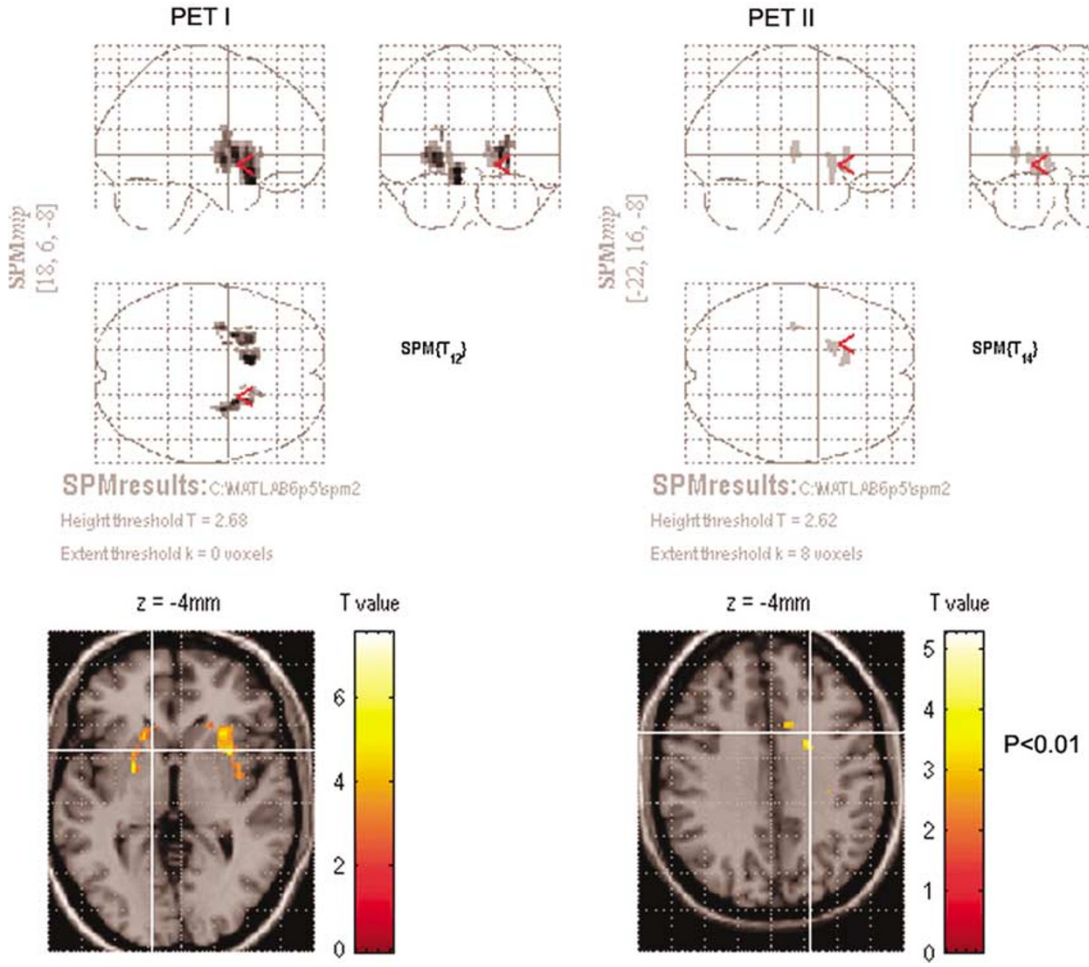

Figure 3 SPM99 analysis. 2D maps and one representative axial view of the clusters of significant reduction of [^{11}C]Rac BP in the basal ganglia of OCD patients evaluated during naïve conditions (PET-I) and during fluvoxamine treatment (PET-II) in comparison with normal controls (unpaired t-test, p threshold = 0.01).

subjects examined in the VST and in seven out of eight patients in the DCA and DPU with a mean increment higher than that previously observed in reproducibility studies. In fact, using a similar data analysis in normal subjects, a reproducibility ranging from −7 to 8% has been reported (Volkow *et al*, 1996).

Imaging studies on SSRI effect in normal subjects reported: (a) increase (Dewey *et al*, 1995; Penttilä *et al*, 2004), (b) no changes (Fowler *et al*, 1999), or (c) decrease (Tiihonen *et al*, 1996) in D_2 receptors availability. In agreement with the results of our study, an increase in D_2 receptors availability was observed in patients with major depression responder to SSRIs therapy but not in nonresponder patients (Klimke *et al*, 1999; Larisch *et al*, 1997). In the present study on OCD patients, we failed to find any correlations between the degree of clinical response and the increase in tracer BP. However, the group of OCD patients evaluated in our study is probably to small to find any correlation between BP and clinical modifications or to separate responder from nonresponder patients. In particular, of the eight patients recruited only one was fully nonresponder at the time of the second PET study. Interestingly, in that patient, the increase in receptors availability was confined to the ventral striatum and not to the dorsal aspect of the basal ganglia.

The mean increase observed in our study is in line with rodent studies indicating an increase in central DA D_2-like receptor function induced by repeated administration of SSRIs (Ainsworth *et al*, 1998a). The same authors also reported an increase in D_2 receptor mRNA and protein expression that was particularly evident in the shell region of rat nucleus accumbens (Ainsworth *et al*, 1998b). [^{11}C]Rac binding has been proven to be sensitive to modification in extracellular concentration of exogenous or endogenous dopamine (Seeman *et al*, 1989; Laruelle, 2000a). Thus, changes in the *in vivo* binding of [^{11}C]Rac could be related either to modifications in receptors expression or extracellular levels of dopamine. This property of [^{11}C]Rac binding, has been used, as an innovative strategy, to measure in living human subjects the modification in extracellular/synaptic dopamine concentration induced by pharmacological or behavioral stimulations (Laruelle, 2000b; Koepp *et al*, 1998). A complex interaction between serotonin and dopamine system has been extensively described also using emission tomography techniques. In particular, serotonin neurons have been found to modulate striatal dopamine release (Dewey *et al*, 1995). The basal firing of dopamine neuron rising from ventral tegmental area is negatively modulated by SSRIs (Di Mascio *et al*, 1998). Microdialysis studies in rats and monkeys indicate that SSRI reduce striatal dopamine levels (Dewey *et al*, 1995; Di Rocco *et al*, 1998; Smith *et al*, 2000) and some of SSRIs side effects have been associated with the reduction of striatal dopamine levels induced by their administration (Damsa *et al*, 2004; Shioda *et al*, 2004). Thus in the light of these results, the increase in receptors availability observed in this study, may be consequent to the reduction of dopamine concentration induced by fluvoxamine. This speculation is also in line with other preclinical and imaging findings indicating an increased dopaminergic tone in OCD striatum. In particular, (a) the administration in rodents of dopamine mimetic such as amphetamine, cocaine induces some stereotypic behaviors that resemble obsessive behaviors observed in OCD patients (Goodman *et al*, 1990; Grace, 2000; Pitman, 1989); (b) the increase in dopamine transporter (DAT) density reported in two out of three different SPET studies on OCD patients (Cheon *et al*, 2004; Kim *et al*, 2003; Pogarell *et al*, 2004).

Finally, fluvoxamine treatment increases D_2 receptors availability in OCD patients reporting striatal BP to values closer to those observed in normal volunteers. This observation is in line with the reduced D_2 receptors availability recently reported in drug-free OCD patients (Denys *et al*, 2004) and suggests that the increase in BP induced by fluvoxamine represents more a normalization than an increase of D_2 receptors availability.

The major finding of the study is that fluvoxamine treatment increases D_2 receptors availability in the dorsal and ventral striatum of OCD patients responder or partial responder to SSRI therapy. The group evaluated in our study is too small to make any conclusion on the role played by dopaminergic system or by dopamine receptors in the efficacy of SSRIs treatment in OCD patients. However of particular interest are the observations that (a) after fluvoxamine treatment, OCD patients have mean BP values closer to those of normal volunteers; (b) in the fully nonresponder subjects, we failed to find any increase in BP values in the dorsal part of the basal ganglia. These findings suggest that in OCD patients, fluvoxamine treatment normalized D_2 receptors availability and also with the limit of a single subject observation, this normalization is not present in the dorsal striatum of the full nonresponder patient. To conclude, our results indicate that dopamine system is modified by the SSRI fluvoxamine and represent interesting informations to be used as starting point for further researches on the role played by dopamine in OCD.

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