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PET Measurements of Neuroreceptor Occupancy by Typical and Atypical Neuroleptics

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The goal of this study was to use PET and ^{11}C-N-methylspiperone (^{11}C-NMSP) to measure the differences in relative occupancy of serotonin (5-hydroxytryptamine-2 or 5-HT$_{2A}$) and dopamine-2 (D2) neuroreceptors in subjects being treated with typical or atypical antipsychotic drugs. **Methods:** We used PET and single-dose ^{11}C-NMSP to measure receptor indices and relative receptor occupancy of 5-HT$_{2A}$ receptors in frontal cortex and D2 receptors in basal ganglia in five subjects who were neuroleptic free, five subjects who were being treated with typical antipsychotic drugs and five subjects who were being treated with clozapine, an atypical antipsychotic drug. **Results:** Among the three groups, there were significant differences in 5-HT$_{2A}$ indices, D2 indices and the ratio of 5-HT$_{2A}$ to D2 indices. With no overlap, the 5-HT$_{2A}$ index separated all subjects who received clozapine and the D2 index separated the remaining two groups. **Conclusion:** Typical antipsychotic and atypical antipsychotic subjects do have differing patterns of 5-HT$_{2A}$ and D2 relative receptor occupancy when measured with a single PET scan, single ^{11}C-NMSP radiotracer dose and no separately injected "cold" pharmaceutical.

Key Words: PET; carbon-11-N-methylspiperone; neuroreceptor occupancy

J Nucl Med 1996; 37:1122–1127

Received Mar. 24, 1995; revision accepted Nov. 1, 1995.

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In vitro N-methylspiperone (NMSP) has been characterized as a high affinity dopamine-2 (D2) receptor ligand in rat and human caudate (*1*) as well as a serotonin-2 (5-hydroxytryptamine-2 or 5-HT_{2A}) receptor ligand in rat and human frontal cortex (*1*). NMSP has been characterized in vivo as a D2 and 5-HT_{2A} ligand in mice (*2*), baboons (*3,4*) and humans (*5,6*). [In accordance with the Serotonin Receptor Nomenclature Committee (*7*), 5-HT_{2A} will be the notation used for receptors previously denoted as 5-HT_2.]

In 1983, Wagner et al. (*5*) reported the use of ^{11}C-NMSP with PET to image D2 receptors in human basal ganglia. Subsequently, Wong et al. (*8*) reported that the ratio of striatal counts to cerebellar counts linearly increased with time in more than 100 normal volunteers and patients administered ^{11}C-NMSP. Wong et al. (*8*) suggested that the slope of this line was related to the rate constant for ^{11}C-NMSP binding to D2 receptors in a three-compartmental model. They also reported that the ratio of frontal cortex counts to cerebellar counts did not linearly increase and reached a relative maximum at approximately 15–45 min after injection (*8*). The value of this ratio at its relative maximum was used as a measure of ^{11}C-NMSP binding to 5-HT_{2A} receptors.

By imaging with ^{11}C-NMSP before and after acute administration of antipsychotic drugs with D2 receptor antagonism, Wong et al. (*9*) demonstrated a dose-related decrease in the slope of the linear regression of the time plot for the striatum/cerebellum ratio. With haloperidol, for example, a single acute dose of 0.05 mg/kg in six normal controls resulted in this D2 receptor index decreasing by 68% in a repeat PET scan. Differences in these ratio indices between a drug treated group and a drug free group can also be used as a measure of relative percent occupancy of neuroreceptors by chronically administered antipsychotic drugs (*10*).

Dysfunction in serotonergic or dopaminergic neurotransmission has been implicated in the pathophysiology of psychosis and other psychiatric illnesses. The efficacy of some drugs used to treat psychosis is related to their ability to alter serotonergic or dopaminergic dysfunction. Investigators have thus used spiperone labeled with different radionuclides to study receptor density in psychiatric patients (*11,12*) or to study relative receptor occupancy by antipsychotic drugs (*13–17*).

Most of these studies focused on either 5-HT_{2A} receptor occupancy or D2 receptor occupancy. Some atypical antipsychotic drugs, such as clozapine, produce high occupancy of 5-HT_{2A} receptors and low occupancy of D2 receptors, while the reverse is true of typical antipsychotic drugs. Meltzer (*18,19*) suggested that the superior efficacy and low extrapyramidal side effects of clozapine may be related not to absolute receptor occupancy of the individual 5-HT_{2A} and D2 receptors but to the extent of 5-HT_{2A} receptor occupancy relative to D2 receptor occupancy.

This study was designed to use ^{11}C-NMSP as a single radiotracer to examine relative receptor occupancy produced by clozapine and by typical antipsychotic drugs of 5-HT_{2A} receptors in frontal cortex and of D2 receptors in basal ganglia to test the hypotheses that: (a) the 5-HT_{2A} receptor indices for clozapine would be lower than those for typical antipsychotic drugs, indicating greater relative occupancy of 5-HT_{2A} receptors in frontal cortex by clozapine; (b) the D2 receptor indices for typical antipsychotic drugs would be lower than those for clozapine, indicating greater relative occupancy of D2 receptors in basal ganglia by typical antipsychotic drugs; and (c) the ratio of 5-HT_{2A}/D2 receptor indices would be significantly lower for clozapine than for typical antipsychotic drugs.

MATERIALS AND METHODS

Subjects

All subjects gave informed consent. Their age and sex are listed in Table 1. The subjects were divided into three groups. Group 1 (n = 5) consisted of two normal volunteers who had never been treated with neuroleptics (Subjects 1 and 2) and three patients (Subjects 3 and 4 with schizophrenia and Subject 5 with bipolar disorder) who had been neuroleptic-free for a minimum of seven days, a time interval beyond which brain receptor occupancy has been reported to be essentially zero (*13*). Group 2 (n = 5) consisted of patients with schizophrenia who were being treated with clinically effective doses of typical antipsychotic drugs. The specific drugs and dosages are listed in Table 1. Group 3 (n = 5) consisted of five patients with schizophrenia who were being treated with clinically effective dosages of clozapine. All patients in Groups 1 and 2 were male. In Group 3, there were two men and three women. Mean ages ± s.d. for Groups 1, 2 and 3, respectively, were 33.0 ± 6.3 yr, 29.2 ± 11.1 yr and 38.6 ± 6.2 yr. Mean dosages in millicuries of ^{11}C-NMSP, ± s.d., administered to groups 1, 2 and 3, respectively, were 16.5 ± 5.4, 18.1 ± 1.5 and 18.5 ± 1.5. Mean specific activities in millicuries per micromole of ^{11}C-NMSP, ± s.d., administered to Groups 1, 2 and 3, respectively,

TABLE 1
Data for Individual Subjects

Subject no.	Total daily dose of neuroleptic	Age (yr)	Sex	5-HT_{2A} index	5-HT_{2A} r.o. %	D2 Index × 10^{-2}/min	Correlation for D2 regression line	D2 r.o. %	5-HT_{2A}/D2 × 10^2 min
1	Neuroleptic-free	33	M	0.93	Baseline	5.83	0.98	Baseline	0.15
2	Neuroleptic-free	36	M	0.48	Baseline	3.80	0.97	Baseline	0.12
3	Neuroleptic-free	31	M	0.52	Baseline	4.15	0.90	Baseline	0.12
4	Neuroleptic-free	24	M	0.83	Baseline	4.23	0.99	Baseline	0.19
5	Neuroleptic-free	41	M	0.51	Baseline	4.86	0.97	Baseline	0.10
6	Trifluoperazine 15 mg	18	M	0.51	32	1.37	0.85	71	0.37
7	Haloperidol 10 mg	31	M	0.62	13	2.49	0.98	43	0.25
8	Perphenazine 48 mg	43	M	0.32	49	2.14	0.73	46	0.15
9	Perphenazine 24 mg	18	M	0.65	07	3.38	0.98	32	0.19
10	Haloperidol 10 mg	36	M	0.38	47	2.34	0.72	45	0.16
11	Clozapine 900 mg	33	M	0.07	86	3.39	0.98	22	0.02
12	Clozapine 350 mg	39	F	0.22	78	5.01	0.98	15	0.04
13	Clozapine 300 mg	48	F	0.22	76	3.62	0.95	34	0.06
14	Clozapine 775 mg	33	F	0.22	79	4.15	0.91	30	0.05
15	Clozapine 500 mg	40	M	0.16	74	3.09	0.98	27	0.05

were 1099 ± 294, 1658 ± 1289 and 1812 ± 1587. No significant age differences, ^{11}C-NMSP dosage differences, or ^{11}C-NMSP specific activity differences between the groups were found.

PET Imaging

All PET scans were performed on a modified Scanditronix SP-3000 scanner. Each scan provided seven slices with a FWHM in-plane resolution of 5 mm and a z-axis resolution of 14 mm.

Subjects were placed supine on the scanning table. The head was held in place with a mask individually molded for each subject from warmed hexalite and attached to the scanning table. Intersecting laser beams were used to align and position the subject according to external canthomeatal and nasal bridge mask markings. Positioning resulted in the first transaxial slice being parallel to and 4 mm below the canthomeatal line (CML). The room was darkened and extraneous noise was minimized. Carbon-11-NMSP was produced by a modification of the method of Dannals et al. (*20*) and administered as an intravenous bolus. Image sampling in list mode began simultaneously with the injection and continued for 60 min.

Analysis of PET Images

Reconstructed images provided tracer concentration for each pixel in units of uCi/cc. After reconstruction, slice selection and region of interest (ROI) placement were performed on a computer by a trained operator (EDM) who was blinded to the clinical data. From the seven transaxial slices, all of which were parallel to the CML, one slice was selected through the basal ganglia and frontal cortex and another slice was selected through the cerebellum. Cortical ROI data was obtained by applying an automated cortical peel technique to the slice through the frontal cortex and basal ganglia (*21*). Geometric regions of fixed shape and size were used for subcortical and cerebellar ROIs. For each of the 15 subjects, scan slices from the total 0–60-min image interval were used for ROI placement. Then the ROIs were applied to each of the smaller time bins in order to construct time plots with the ROI ratios.

From the above described time plots, the technique of Nyberg et al. (*22*) was used to obtain a 5-HT$_{2A}$ index for each subject. In this technique, $C_b(t)$ is tracer concentration specifically bound to the 5-HT$_{2A}$ receptors in frontal cortex; $C_{fr}(t)$ is the total of both specific and nonspecific binding of tracer concentration in frontal cortex; $C_{cer}(t)$ is tracer concentration in cerebellum and is used as a measure of nonspecific binding. $C_b(t)$ is defined as the difference between $C_{fr}(t)$ and $C_{cer}(t)$:

$$C_b(t) = C_{fr}(t) - C_{cer}(t).$$

The 5-HT$_{2A}$ index is defined as:

$$I_{5\text{-Ht2A}} = \int_9^{45} C_b(t)\,dt \Big/ \int_9^{45} C_{cer}(t)\,dt.$$

The lower and upper limits on the integrals were set at 9 and 45 min to correspond to the 9–45-min integration of Nyberg et al. (*22*). While the lower limit of 9 min has the disadvantage of steady state not yet always being achieved, we chose to maintain this limit so that data from this study could be more directly compared to that of Nyberg et al. (*22*).

The technique of Wong et al. (*7*) was used to obtain a D2 index for each subject. In this technique, average tracer concentration per pixel in each of the above described time bins was computed for the ROI in basal ganglia and the ROI in cerebellum. A linear regression analysis was applied to the ratio of these values across the time bins. In this particular three-compartment modeling approach, k_2 was assumed to be considerably greater than k_3 and the D2 index was defined as the slope of the regression line. The 5-HT$_{2A}$ and D2 indices were age corrected for males and females

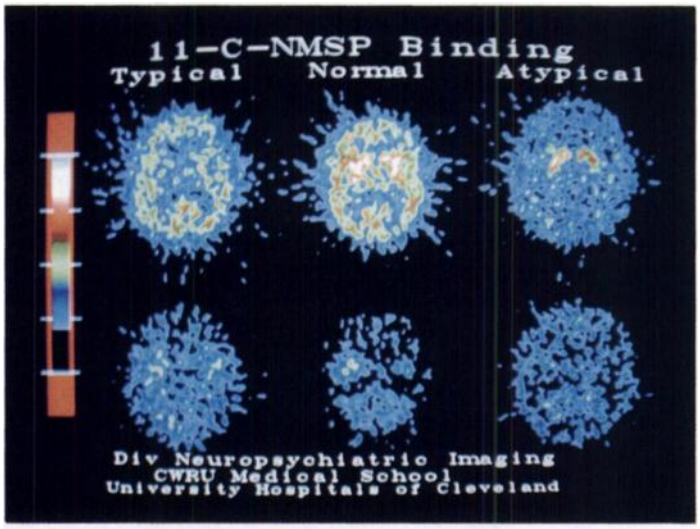

FIGURE 1. Carbon-11-NMSP transaxial images with nonspecific binding in cerebellum set at the same grey scale of 25% of the color bar. All other intensities above 25% of the color bar are linearly proportional. Top row images include the basal ganglia and frontal cortex and the bottom row images include the cerebellum for (left to right) a patient receiving trifluoperazine, a normal volunteer and a patient receiving clozapine.

using normative data from Wong et al. (*7*), (Figs. 3, 6) to derive linear correction factors. These 5-HT$_{2A}$ and D2 receptor indices vary inversely with the degree of binding by the antipsychotic drug so that a greater degree of receptor binding results in lower indices (*7,22*).

The mean values of the 5-HT$_{2A}$ and D2 indices for the neuroleptic free subjects (Group 1) were considered as measures of baseline occupancy for 5-HT$_{2A}$ and D2 receptors, respectively. The numerator for the relative percent occupancy for each subject in the antipsychotic drug groups for the 5-HT$_{2A}$ and D2 receptors is the difference between the mean 5-HT$_{2A}$ or D2 baseline index and their individual 5-HT$_{2A}$ or D2 index, respectively. The denominator is the mean baseline 5-HT$_{2A}$ or D2 index, respectively.

Indices for 5-HT$_{2A}$, D2 and the ratio of 5-HT$_{2A}$/D2 were compared among the neuroleptic free group, the typical antipsychotic drug group and the atypical antipsychotic drug group using an analysis of variance (ANOVA). Subsequent pairwise comparisons were by two-tailed t-tests. To address issues of unequal variance, nonparametric analyses, using Kruskal-Wallis and Mann-Whitney U statistics, were also performed.

RESULTS

The age, sex and total daily dosage of neuroleptic for each subject are listed in Table 1. Sample images from Subjects 6, 1 and 11 in Table 1 (selected from Groups 2, 1 and 3, respectively) are illustrated in Figure 1. The illustrated images are taken from a 5-min time bin with an average midpoint of 44 mins after injection. The normal subject in the center of the images provides a reference for the extent of ^{11}C-NMSP binding to 5-HT$_{2A}$ receptors in cortex and to D2 receptors in the striatum. Compared to the normal subject, the patient treated with a typical neuroleptic showed markedly diminished intensity in the striatum. This is consistent with a high relative occupancy of D2 receptors by trifluoperazine. Some visible decrease in cortical binding is also evident, suggesting a lower relative occupancy of 5-HT$_{2A}$ receptors. In the patient treated with clozapine, there is markedly diminished intensity in the cortex compared to the normal control. This is consistent with a high relative occupancy of 5-HT$_{2A}$ receptors. There is also some decrease in striatal intensity compared to the normal control, indicating a lower relative occupancy of striatal D2

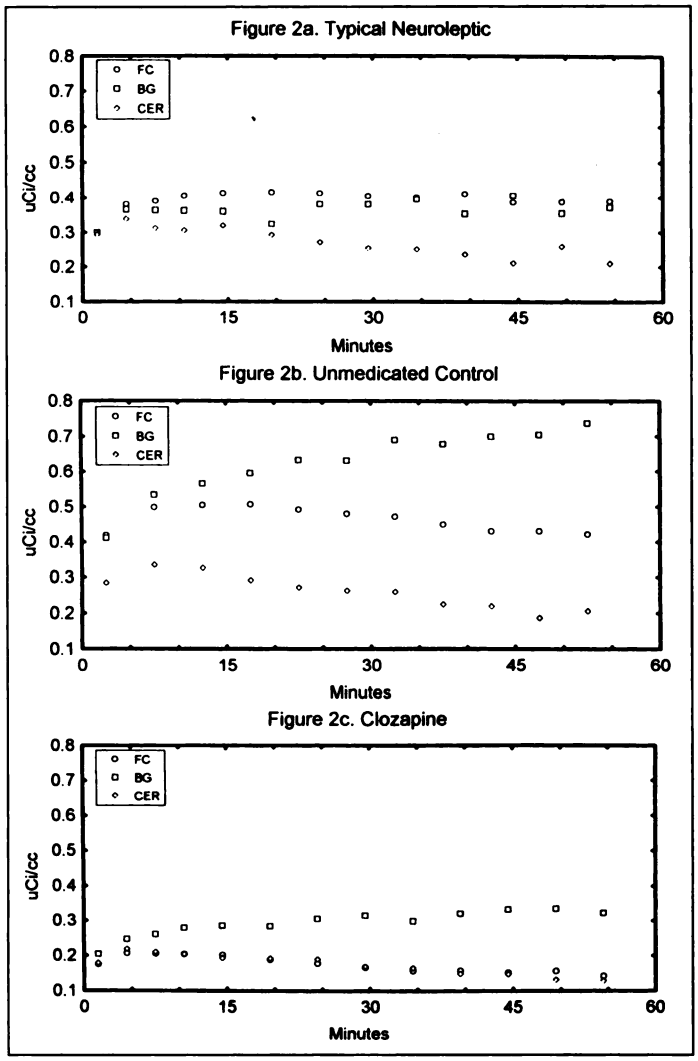

FIGURE 2. Activity (μCi/cc) versus time for ROIs in the frontal cortex (FC), basal ganglia (BG) and cerebellum (CER) for subjects from the typical, control and atypical groups.

receptors. Time-activity curves for the frontal cortex, striatum and cerebellum for subjects in Figure 1 are illustrated in Figure 2.

The 5-HT_{2A} and D2 indices of the two normal controls (subjects 1 and 2) bracket the three neuroleptic-free patients (Subjects 3, 4 and 5), indicating no residual effects on these indices from prior neuroleptic treatment. The following results are illustrated quantitatively in Table 1:

1. The 5-HT_{2A} index separates subjects who received clozapine from those who were either neuroleptic-free or who received typical antipsychotic drugs. Specifically, all subjects who received clozapine had a 5-HT_{2A} index $\leq$0.22, while those who were neuroleptic-free or who received typical antipsychotic drugs had 5-HT_{2A} indices $\geq$0.32.
2. The D2 index separates all subjects who received typical antipsychotic drugs from those who were neuroleptic-free. Specifically, all subjects who received typical antipsychotic drugs had a D2 index $\leq 3.38 \times (10^{-2}\ \text{min}^{-1})$, while all subjects who were neuroleptic-free had a D2 index $\geq 3.80 \times (10^{-2}\ \text{min}^{-1})$. The D2 index did not separate individual subjects who received typical antipsychotic drugs from those who received clozapine.
3. The ratio of the 5-HT_{2A}/D2 indices, like the 5-HT_{2A} indices, separates those subjects who received clozapine from those who were neuroleptic-free or who received typical antipsychotic drugs. Specifically, all subjects who received clozapine had a 5-HT_{2A}/D2 ratio $\leq 0.06 \times 10^2$ min, while all subjects in either of the other two groups had a ratio value $\geq 0.10 \times 10^2$ min.

Listed in Table 2 are the group means and s.d. for both the 5-HT_{2A} and D2 indices, the ratios of the 5-HT_{2A} and D2 indices and the relative percent occupancy of the 5-HT_{2A} and D2 receptors for the neuroleptic-free, typical antipsychotic drug and clozapine groups. ANOVA comparisons of the indices and their ratios are also listed in Table 2. Subsequent pairwise comparisons are listed in Table 3. A summary of these data follows:

1. In the ANOVA, the three groups significantly differed in their 5-HT_{2A} indices. Subsequent pairwise comparisons by two-tailed t-test revealed that the mean 5-HT_{2A} index for the clozapine group was significantly decreased compared to the neuroleptic-free group. The mean for the clozapine-treated group was also significantly decreased compared to the typical antipsychotic drug group.
2. The three groups also differed in their D2 indices. Subsequent pairwise comparisons by two-tailed t-tests revealed that the mean D2 index for the typical antipsychotic drug group was significantly decreased compared to the neuroleptic-free group and the clozapine group. D2 indices were nonsignificantly reduced in the clozapine group compared to the neuroleptic-free group.
3. Additionally, differences appeared in the ratio of the 5-HT_{2A} and D2 indices. Subsequent pairwise comparisons by two-tailed t-test revealed that the mean ratio of indices for the clozapine group was significantly decreased compared to the typical antipsychotic drug group. The ratio was also significantly decreased in the clozapine group compared to the neuroleptic-free group. Nonparametric analyses with Kruskal-Wallis and Mann-Whitney U-statistics confirmed the significance of all results reported above.

Overall, relative percent occupancy of 5-HT_{2A} receptors was 23% for the group treated with typical antipsychotic drugs and

TABLE 2
Results of Neuroleptic-Free Subjects, Patients Treated with Typical Antipsychotic Drugs and Patients Treated with Clozapine

Receptors	Neuroleptic-free indices (mean ± s.d.)	Typical APD indices (mean ± s.d.)	Clozapine indices (mean ± s.d.)	F (2, 12)	p ≤	Typical APD r.o. % (mean ± s.d.)	Clozapine r.o. % (mean ± s.d.)
5-HT_{2A}	0.65 ± 0.20	0.50 ± 0.14	0.18 ± 0.06	12.54	0.001	23 ± 22	72 ± 10
D2	4.57 ± 0.80	2.34 ± 0.72	3.85 ± 0.75	11.21	0.001	48 ± 15	19 ± 10
(5-HT_{2A}/D2)	0.14 ± 0.03	0.22 ± 0.09	0.04 ± 0.01	12.16	0.001	-	-

APD = antipsychotic drugs.

TABLE 3
Two-Tailed t-Test Probability Values

Receptors	Neuroleptic-free vs. typical APD	Neuroleptic-free vs. clozapine	Typical APD vs. clozapine
5-HT_{2A}	$t = 1.35, p \geq 0.211$	$t = 4.81, p \leq 0.002$	$t = 4.43, p \leq 0.003$
D2	$t = 4.62, p \leq 0.002$	$t = 1.47, p \leq 0.178$	$t = 3.22, p \leq 0.013$
5-HT_{2A}/D2	$t = 1.91, p \geq 0.100$	$t = 5.51, p \leq 0.001$	$t = 4.30, p \leq 0.003$

APD = antipsychotic drugs.

72% for the group treated with clozapine. Relative percent occupancy of D2 receptors was 48% for the group treated with typical antipsychotic drugs and 19% for the group treated with clozapine.

DISCUSSION

Several investigators have used the approach where a control group mean is utilized as the baseline index for occupancy calculations of the 5-HT_{2A} and D2 receptors. For example, Farde and Nordstrom (*23*) used this approach with ^{11}C-raclopride to measure D2 receptor occupancy in basal ganglia. They found a mean occupancy ± s.d. of 48% ± 11% in five patients treated with clozapine and a mean occupancy of ± s.d. 78% ± 6% in 22 patients treated with typical antipsychotic drugs. In a more recent article by this group (*24*), the original sample of five patients on clozapine was expanded to include 11 additional patients. Although four of these subjects, like our five subjects, had relative D2 occupancies ≤34%, the mean occupancy was similar to their earlier published results (mean ± s.d. = 47% ± 16%). These mean values, differ from our mean values for D2 relative percent occupancy of 19% for clozapine and 48% for typical neuroleptics. The differences may be related to their usage of the radiotracer ^{11}C-raclopride with its associated different modeling techniques to measure D2 occupancy versus our usage of ^{11}C-NMSP. For example, if k_2 is not considerably greater than k_3, then usage of the single radiotracer ^{11}C-NMSP and single scan technique to quantitate D2 receptor occupancy may result in occupancy values for D2 receptor occupancy which are lower than those obtained with ^{11}C-raclopride.

When the Karolinska group used ^{11}C-NMSP to measure 5-HT_{2A} receptor occupancy with the same modeling equations as were applied in this study, their results were similar to ours. Specifically, Nordstrom et al. (*25*) measured 5-HT_{2A} receptor occupancies in frontal cortex of three patients treated with clozapine and calculated values of 84%, 87% and 90%. In a later article, two more patients were added with relative occupancies of 92% and 94%.

Since spiperone and clozapine bind to both D2 and D4 receptors, the single scan technique described in this article cannot differentiate between D2 and D4 receptor occupancy. Differentiation of D2 and D4 receptor occupancy would thus require an additional scan with a radiotracer such as raclopride which is significantly more specific for the D2 receptor than for the D4 receptor. Another limitation of this one scan technique is that it does not provide quantification of B_{max} and/or K_D. Wong et al. (*26*) reported using ^{11}C-NMSP to obtain quantification of B_{max} and K_D for the D2 receptor, but this requires an indwelling arterial catheter and a repeat scan following acute administration of a nonradioactive D2 receptor blocker. Once B_{max} or K_D is obtained, however, percent occupancy calculations still require a ratio of some type of baseline off drug values and on drug values. Nonetheless, in the current study, we have used the terminology "relative" receptor occupancy to distinguish this one scan technique from multi-scan techniques with indwelling arterial catheters and acute administration of "cold" pharmaceutical.

Since radiotracers, PET scanners, PET procedures and data analysis techniques differ among different centers, it is possible that relative percent occupancy measures as well as relative 5-HT_{2A} indices and D2 indices may also differ. Data in this study, however, seem to indicate that it is possible, within the same laboratory (and possibly with future verification studies across several laboratories), to establish definitive ranges such that these relative measures distinguish between individuals who are neuroleptic free, being treated with typical antipsychotic drugs or being treated with clozapine. These differences were obtained without subjecting the patients to an arterial line, multiple scans, multiple dosages of the same or differing radiopharmaceuticals or to administration of "cold" pharmaceuticals between repeat scans. Not having an arterial line, repeat scans or multiple radiotracer administration has "user-friendly" advantages for the patient. Additionally, the ability to obtain quantitative differences without administering a separate dosage of "cold" pharmaceuticals after the first radioactive scan and then subsequently repeating a scan with radioactive tracer could be important in those protocols which do not permit any usage of active drug other than the one undergoing the protocol trial.

CONCLUSION

Typical antipsychotic and atypical antipsychotic subjects do have differing patterns of 5-HT_{2A} and D2 relative receptor occupancy when measured with a single PET scan, single ^{11}C-NMSP radiotracer dose and no separately injected "cold" pharmaceutical.

ACKNOWLEDGMENTS

We thank Ms. Emily Wilson for her assistance in preparing the ^{11}C-N-methylspiperone. This study was supported in part by grants from the Cleveland Foundation (PFG, WES, SCS), National Association for Research in Schizophrenia and Depression (PFG, WES), Heart and Lung Institute NIH 43884 (MSB), Laureate and Elizabeth Prentiss Foundation (HYM), USPHS MH 41684 (HYM) and U.S. Public Health Service Research Career Scientist Award MH 47808 (HYM).

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Skeletal Muscle Uptake of Fluorine-18-FDG: Effect of Oral Diazepam

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We have observed a pattern of symmetrically increased uptake of [^{18}F]fluorodeoxyglucose (FDG) in the neck and thoracic paravertebral regions of several patients referred for whole-body PET. The distribution is suggestive of uptake in contracting skeletal muscle in tense patients. **Methods:** To test this hypothesis, six successive patients who exhibited this pattern of uptake underwent rescanning using an identical imaging protocol but with oral diazepam before injection of FDG. **Results:** The increased neck and paravertebral uptake was significantly reduced or abolished with diazepam, confirming the supposition that this increased neck and paravertebral uptake represents a normal variant of muscle uptake. **Conclusion:** Oral diazepam given before the uptake period can be helpful in such patients to exclude the masking of potential abnormalities by this characteristic pattern of FDG uptake.

Key Words: fluorine-18-fluorodeoxyglucose; muscles; glucose metabolism; diazepam

J Nucl Med 1996; 37:1127–1129

Whole-body [^{18}F]-fluorodeoxyglucose (FDG) PET is used in oncology to stage patients at initial presentation and to assess tumor recurrence and the effects of therapy (*1–3*). We have observed a distinctive pattern of symmetrical uptake of FDG in the neck and thoracic paravertebral region of several patients referred for whole-body imaging. The distribution is suggestive of uptake in contracting skeletal muscle in tense patients, but can be of sufficient intensity to mask true potential sites of disease, particularly in the cervical and supraclavicular regions. To test our hypothesis that this uptake was physiological, we rescanned six patients who exhibited this pattern of FDG uptake after administration of oral diazepam.

Received Mar. 8, 1995; revision accepted Sept. 12, 1995.
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MATERIALS AND METHODS

Patients

Consecutive patients referred for whole-body scans between March 1994 and April 1995 who exhibited symmetrical FDG uptake in the neck or paravertebral region were recalled within 6 wk of their initial scan for repeat imaging. Referring clinicians were advised that repeat scans were required to assess whether the uptake represented pathological lymph node involvement or normal muscle activity. The patients did not receive any treatment in the interval between scans. The indications for initial scanning in five patients restudied were to assess the effects of chemotherapy. Two patients were thought to be clinically free of disease (one with a synovial sarcoma treated with surgery and chemotherapy; one with symptomatic improvement after chemotherapy for an infiltrative brachial plexopathy due to breast carcinoma). Three patients with Hodgkin's disease underwent rescanning because specific sites of clinical concern were thought to represent active disease (one with persistent induration in the right supraclavicular fossa; one with persistently enlarged axillary lymph nodes; one with a residual mediastinal mass on CT). Another patient with neurofibromatosis underwent scanning at the routine follow-up visit after surgical excision of a midthoracic sarcoma 12 mo earlier.

Imaging

The preparation and imaging protocol for both studies were identical, but on the second occasion each patient received 5–10