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and work on the Cluster Impact project that was more [redacted] cussed.

The Committee found a num[redacted] used the facilities well and show promise of cont[redacted] In particular, the facilities promote excellent

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A Regional Cyclotron-PET Center for Radiotracer Research and Medical Application; Cocaine Analogs for PET Studies of Synaptic Activity; High-Field Magnetic Resonance Imaging

J. S. Fowler, A. P. Wolf, S. L. Dewey, Y.-S. Ding, R. A. Ferrieri, M. L. Firouzbakht, S. J. Gatley, A. V. Levy, J. Logan, D. J. Schlyer

The PET-cyclotron team at Brookhaven National Laboratory continues to produce outstanding research and is one of the most highly productive and regarded PET facilities in the nation. The program focuses on developing PET imaging techniques to conduct basic and clinical research with applications for substance abuse, interactions of brain neurochemical pathways and drug research. The program has been strengthened since the last review period by expansion of its research capabilities. The highlights of this expansion include 1) the acquisition of a high field (4 T) MRI instrument, 2) the development of novel drugs and radioreceptor assays to screen them, 3) the development of *in vivo* microdialysis techniques to examine release of neurochemicals subsequent to drug administration. Each of these additions to the program has increased the capability of a systematic approach to neuroscience research.

The original team was assembled by Dr. A. Wolf and clearly excelled in its mandate. Under Dr. J. Fowler's leadership, the team not only has maintained its high level of productivity, quality and relevance but continues to expand into new areas and develop novel programs. Her leadership is exemplary and the interaction with Dr. Volkow in the Medical Dept. continues to produce exciting and important advances.

The team has made impressive progress in the last two years in its ongoing studies. These include the synthesis of novel radionuclides, radioligands,

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improvements in ^{18}F production, exploration of psychostimulant targets in brain (e.g. the dopamine transporter), neurotransmitter interactions, neurotransmitter analog processing in heart and normal ageing. Recent highlights are the synthesis of methylphenidate derivatives, [^{11}C]methylphenidate for PET imaging, and ^{18}F-catecholamines by Dr. Yu-Shin Ding. The latter compounds were subsequently used in neurocardiology research to measure clearance rates from the heart. The synthesis of the active and inactive enantiomers of methylphenidate facilitated the development of a selective and important ligand for PET imaging of the dopamine transporter. Of particular interest was the observation by PET techniques, that the stimulants cocaine and methylphenidate, were distinguishable. A temporal dissociation was observed between receptor occupancy and production of a subjective "high" by methylphenidate contrasted to results with cocaine. For cocaine, the time of occupancy of the dopamine transporter correlated with the production of subjective effects. Such findings have implications for the mechanism of action of stimulant drugs. The duration of action of deprenyl, a potential drug therapy for Parkinson's disease was determined by PET imaging and a kinetic model developed by Dr. Logan. The successful development of microdialysis techniques by Dr. Dewey strengthened the overall program and supported conclusions drawn from PET imaging studies designed to uncover neurotransmitter interactions. This technique also was used to evaluate novel methylphenidate analogs. The development of radioreceptor assays to evaluate the affinity and selectivity of novel drugs by Dr. Gatley were successfully incorporated into the drug development program. The Department is to be commended for rapid development and utilization of these techniques for new and important initiatives. Impressive progress was made by Dr. Levy on improving techniques for localizing brain regions acquired by imaging techniques.

Another highlight of the program is the acquisition of high-field magnetic resonance imaging capability. Under the leadership of Dr. Springer, who is highly qualified for this position, the program is destined to be indispensable as a

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support for the PET imaging effort but, more importantly, as an instrument for development of pioneering imaging methods. In summary, the program not only continued its high quality and productive research but expanded the scope of problems that can be addressed by acquiring new techniques and instrumentation and synthesizing novel drugs.

In addition to DOE support, the group is funded by other sources which include NIH/NINDS/NIDA/NIAAA, NARSAD and Hoffmann-LaRoche. The investigators have established extensive collaborations with SUNY and NYU, seven hospitals (4 V.A.), and a pharmaceutical company.

The PET-cyclotron team continues to be highly productive and maintain its standards of excellence and relevance. The expansion of chemical, biological and imaging capabilities not only has enhanced the creative capacities of the group but also has provided means to confirm what was inferred from results of PET imaging. One of the great strengths of the PET-cyclotron team is their ability to cooperate and pool research efforts and ideas. Their success clearly reflects Dr. Fowler's leadership and expectations. Such cooperativity is essential for maintaining the high standards of excellence and productivity of the team. It is essential that all team members be willing to contribute as a team member.

Based on current use of the PET camera (400 studies/year) and the number of individuals requiring camera time to pursue various projects, it is strongly suggested that the laboratory acquire another PET camera.

The Department also should consider intensifying the effort in SPECT imaging techniques.

A committee, composed of BNL personnel and outside consultants, should formulate a plan for use of the new MRI instrument, one that includes objectives, users and time allocation. Such a plan should be developed within the next two years in order to maximize use of this facility.

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