Final Examination of

Kathryn Estelle Gill

For the Degree of

DOCTOR OF PHILOSOPHY

December 2013
Winston-Salem, NC

COMMITTEE IN CHARGE

Beth A. Reboussin, Ph.D., Chairperson
Linda J. Porrino, PhD., Advisor
Thomas J.R. Beveridge, Ph.D.
Michael A. Nader, Ph.D.
Jeffrey L. Weiner, Ph.D.

PTCRC - Auditorium
October 16, 2013
9:00 a.m.
PROFESSOR(S) IN CHARGE OF RESEARCH
Linda J. Porrino, Ph.D.
Professor and Chair
Department of Physiology and Pharmacology

FIELDS OF GRADUATE STUDY
Major Subject: Physiology and Pharmacology
Neuroscience, Pharmacology, Substance Abuse

SUMMARY OF DISSERTATION

METHYLPHENIDATE TREATMENT AND REARING ENVIRONMENT:
EFFECTS ON THE DOPAMINE SYSTEM AND VULNERABILITY TO SUBSTANCE
ABUSE IN ANIMAL MODELS

The purpose of these studies was to investigate the effects of chronic methylphenidate treatment, at
doses that have been associated with clinical efficacy in children, on the dopamine system and
vulnerability to substance abuse in animal models. Methylphenidate is the most commonly
prescribed stimulant to treat Attention Deficit Hyperactivity Disorder. As a dopaminergic agent, it
has potential to cause long-term alterations of a neural system that has been associated with
numerous psychopathologies, including substance abuse. Yet, few studies have examined its long
term effects on the brain. Another factor that can influence vulnerability to substance abuse is early
rearing environment, as children raised in negative environments are more likely to develop
substance abuse disorders. These studies examined the interaction of environment and
methylphenidate on the dopamine system and vulnerability to cocaine and alcohol abuse.

Both nonhuman primate and rodent models were used in this series of studies. Nonhuman primates
were treated with an extended release formulation of methylphenidate and rodents were treated with
a consistent subcutaneous infusion of methylphenidate. Rodents were also exposed to different
environmental conditions during the treatment phase. In both species, the age of treatment, duration
of treatment, and doses used were matched as closely as possible to the human condition. Positron
Emission Tomography (in nonhuman primates) and in vitro autoradiography (in rodents) were
employed to evaluate the availability and density of dopamine receptors and transporters.
Nonhuman primates and rodents were then exposed to cocaine and alcohol self administration,
respectively.

Methylphenidate treatment had no effect on the dopamine systems of nonhuman primates or
rodents, though treatment plus drug washout altered the trajectory of D2-like receptor development
in treated nonhuman primates. Social isolation was associated with greater levels of D1-like
receptors in rats. Methylphenidate did not alter vulnerability to cocaine self-administration, but it
did increase ethanol intakes and preferences in socially isolated rodents. In conclusion,
methylphenidate may not have long-term effects on the dopamine system in treated children, but it
may increase vulnerability to substance abuse in a subset of individuals that have a negative
environmental history.
SCHOLASTIC VITAE

EDUCATION

2013 - Ph.D., Physiology & Pharmacology, Wake Forest University School of Medicine, Winston-Salem, NC

2004 B.A., Psychology and French, Wake Forest University School of Medicine, Winston-Salem, NC

AWARDS

2009 – 2011 National Institute of Alcoholism and Alcohol Abuse

2010 Competitive Travel Award

OUTREACH ACTIVITIES

2009-2011 Brain Awareness Council: Organized by graduate students across multiple disciplines at Wake Forest University, the BAC visits local elementary, middle, and high schools, and coordinates with Winston Salem’s SciWorks and the Children’s Museum, to educate children in the areas of comparative brain anatomy, drug addiction, basic neurology, and career opportunities in science.

2009-2011 Neurotransmitter Newsletter: Contributed to this online internal newsletter written by graduate and students and faculty in the neurosciences at Wake Forest to inform and educate the scientific communities on local and national happenings in the Neuroscience world.

2010-2011 Kernersville Cares for Kids: Helped organize visits by local elementary and middle school children to the drug abuse research laboratories at Wake Forest to educate them about drug and alcohol use.

2009-2011 Education on Animal Research: Volunteered to lead tours of middle and high school students around the nonhuman primate research facilities at Wake Forest to educate young students about humane animal research.
PUBLICATIONS


**Abstracts**


