

NIMH IRB MINUTES 10/28/03 FINAL

(B) Principal Investigator:

Protocol Title: Effects of Single Dose of Dextroamphetamine in Attention Deficit Hyperactivity Disorder

Protocol summary: This study includes a double-blind, placebo-controlled challenge with a single low dose of oral dextroamphetamine (10mg) in 14 healthy control children, 14 ADHD children and 12 pairs of monozygotic and dizygotic children discordant for ADHD. An fMRI will follow the medication administration to examine differences between groups.

DISCUSSION:

Dr's _____ were present for the discussion of this protocol.
Dr. _____ provided an overview of the study using the IRB protocol review standards.

Scientific design: This study was reviewed and approved by the CSRP on 9/8/03 for submission to the IRB. _____ described the study in detail, emphasizing the importance of the information in gaining a fundamental understanding of ADHD.

Risks/benefits: Based on previous work by the investigators using single low doses of amphetamine in children, the side effects experienced by the children are likely to be mild loss of appetite, and some degree of activation in healthy children. Therefore, the investigator suggests that this is a minimal risk study.

Subject selection: This study will include children with and without ADHD, and twins discordant for ADHD, aged 9-18.

Additional safeguards for vulnerable subjects: Parents or guardians will be required to provide permission. Children with ADHD and healthy control children will be required to provide assent.

Minimization of risks to subjects: On page 15 of the protocol the investigator outlines study risks and the efforts the researchers will take to minimize them.

Privacy & confidentiality: Confidentiality and privacy will be protected

Consent document: All required elements are included in the consent form.

Additional considerations: This study does not use radiation, is not a collaborative study, and does not require an IND.

The board asked the investigator whether this study could be completed using just children in the older age range (16-18 year olds). The investigator emphasized that most children diagnosed with ADHD are between the ages of 6-12, and that confining the sample to just older-aged children would provide a significant confound for this study.

The board asked the investigators how they will manage movement artifact if the children do not lie still in the scanner. The investigators described the "training" the staff use with the children to acquaint them with the MRI and the testing sessions. These sessions have been highly successful in reducing movement in the scanner.

The board asked about the inclusion of healthy controls with mild past anxiety disorder or depressive episodes. The investigators clarified that they will limit enrollment of control children to adjustment disorder with depressed features, and not include subjects who have been diagnosed with major depression in the past.

The board asked about the investigators' experience with side effects from a single dose of amphetamine in children. The investigator described the variability of response between subject groups, which included healthy children and adults, and children with ADHD. In the group of healthy children there was minimal response to the medication. Some children were reported to have temporary difficulty sleeping, or a poor appetite following medication administration. Otherwise there were no significant effects from the medication in the healthy children. There was one report of hallucinations following exposure to the drug in a child with brain damage exposed to the medication.

Dr's _____ left the meeting at this time.

DISCUSSION IN EXECUTIVE SESSION:

Dr. Rosenstein reviewed with the board Title 45 CFR part 46, subpart D "additional DHHS protections for children." The board then focused their discussion on the risk determination for this study. Members of the board discussed the risk level from two perspectives:

- Discussion supporting the study being designated **greater than minimal risk** focused on the risk of exposing healthy children to a controlled substance that has potential for abuse/addiction. Is it reasonable to expose children, without a condition, to such a substance?
- Discussion supporting designating the study as **minimal risk** focused on the compelling scientific justification for the study, and the opinion that the risk of exposure to this drug, in a "supervised setting" does not exceed the risks children are typically exposed to. Some members of the board felt that the concerns about potential substance abuse risks could be more precisely detailed in the consent/assent forms to better inform parents/children of the potential associated risks. It was also suggested that since the potential for abuse is likely to be greater in older children, the age range of eligible subjects might be limited to those less than 12 years.

IRB DECISION AND VOTE: The board voted initially on whether the research procedures for healthy children were minimal risk, with 6 members voting that it was greater than minimal risk and 4 that it was no greater than minimal risk. A motion was made to table the protocol for further consideration at the next IRB meeting, to allow the board members additional time to review the regulations and consider the risk level determination for this study. There were 5 votes for and 5 votes against this motion (one abstention). As the chair of the IRB, Dr. Rosenstein broke the tie and upheld the motion to defer a final vote on this protocol until the next meeting. This protocol will be the first item on the agenda for the meeting scheduled 11/04/03.