CIFASD MEETING
Westin Bayshore Resort & Marina
Vancouver, BC

Date/Time **June 24- 25, 2004 @ 9:00 P.M. (PST)**

DISCUSSION/RECOMMENDATION
Opening Remarks - NIAAA
Faye Calhoun: FAS is unique – should be making tremendous progress.
Advocacy groups are looking to (us) CIFAD for answers and more information.
We need to present our findings in a well-structured manner.
Ken Warren: Stressed the importance of this project succeeding.
We are on a very tight timeline; awards staggered; stressed a call to further cooperation and a level of productivity on projects.
Need to produce data-more importantly goals.
Achievements have been made that ordinarily could not have been achieved.
Stressed that he and Deidra Roach need to feel a good sense that the project is moving progressively forward.
Deidra Roach: Looking forward to reviewing/seeing project reports.

Review of Clinical Cluster
Dysmorphology Core – Ken Jones
Specific Aim #1: Implementation of a standard protocol to be used at each project site.
Development of a manual to explain and standardize the methods used in performing the physical examination.
Translation of the Dysmorphology Form and manual into Russian and Ukrainian.
Training of local Pediatricians.
4 local Pediatricians to be trained in Moscow
8 Russian Neonatologist and/or Geneticists have been trained in Ukraine
16 Pediatricians, Neonatologist and/or Geneticists have been trained in Ukraine
4 Pediatrician and/or Neurologists have been trained in Rome.
Travel to Consortium sites to verify diagnosis and update training.
Specific Aim #2: To explore extent to which various degrees of deficient anthropometric measurements should be used to enhance specifically of diagnosis without loss of sensitivity.
Considering dropping Specific Aim #2 – Pediatrician office not necessarily the best place to diagnose FAS.
Specific Aim #3: Explore strategies for diagnosis of FASD in the newborn period or at least during the first year of life.
Specific Aim #4: a) Delineation of the full spectrum of defects.
b) Identifying clinical features that are most indicative of future problems in neurobehavioral development.
Specific Aim #5: Correlation of the clinical diagnosis with that determined by 3-D photography.
Significance: 1) Demonstrated our ability to train local Pediatricians.
2) Demonstrated the effectiveness of ascertaining children with FASD in normal 1st grade classes.
3) Developed and field tested a highly effective physical examination form and manual that have been "field tested."
Stressed that getting school systems involved getting neuro-cognitive testing as opposed to FAS testing, allowing teachers and educational psychologist to get in the loop would be very helpful in identifying FAS in the school systems.

Facial Imaging Core – Elizabeth Sowell for Tatiana Foroud
Project Progress:
Cross calibration assessment of the new cameras

- Scanned one model (plastic skull) with all cameras to record differences between them

- Preliminary analysis: cameras are on par with each other with respect to accuracy
- Undergoing more detailed analysis

Acquired a standard model (plastic skull) to "calibrate" cameras at remote sites

- Protocol being developed by Jeff Rogers.

AVL scanned a plaster dental model provided by Dr. Ken Jones to Dr. Fang

- After images are merged, Dr. Fang will analyze the model and use it for quality control.

Imaging problems have been taking more time than expected.
Subject positioning – hard to keep subjects to keep the same position/expression
Lighting – too much for the room size
Movement – too much (0.6 second seems very long), camera beeps.
Face marking – dots too large
Age of subjects – child <2 years of age difficult to scan
Functional ability of subjects – many unable to understand and/or complete simple instructions.
Future Strategies:
Purchase another camera – 2nd year of grant, plan to dedicate it to S. Africa
Camera Itinerary – Buffalo, San Diego, Plains

- Finland-Russia
- Italy
- Indianapolis

Laser is safe enough for children to look directly into it, passes very quickly.
Need for coordination of when and where the cameras will be at and what time.
Jeff, Phil, Gene and Luther have all been trained to use the camera.
Would be willing to send someone to be trained – only takes a couple of hours.
Would like to schedule group training.

Pilot Project Cores

Comparison of 3 Diagnostic Modalities in FASD – Ed Riley for Luther Robinson

Currently on-track to complete study in 2-year time frame.
3-D images have been sent; none sent to brain informatics-awaiting final project.
There is a question whether local morphological data can be expected.
R01 developed.
Initial 4-5 year pilot projects have been cut back to 3 years.

FASD Epidemiology in Italy – Phillip May

There is a shortage of equipment – only 2 cameras available.
Population where testing is taking place, has to agree to the use of the camera.
It was reiterated that training was provided in January, 2004, in Indianapolis.
Prenatal drinking is twice the US studies.
Re: Indian Study Population Wave I - Only receive approximately 50% of consents, because of stigmas regarding physical exams, etc., and in these areas, schools means jurisdiction, not buildings
Testing approved as a study of development, not alcohol.
Trained several medical students and physicians.
Received 90% of samples.
Final case conferences need to be scheduled.

Detecting FASD from Neonatal Ultra Sound – Ann Streissguth

Objective: To develop methods and procedures for the earliest possible detection of babies with prenatal damage from alcohol, using technology that can fit easily into existing health care systems.
Specific Aims: To demonstrate that our method of averaging intra-cranial ultrasound images of the corpus callosum (CC) can differentiate between alcohol exposed and unexposed newborns.
Recruitment: Through community referral and 2-stage screening:

1. Hospital Screening Questionnaire (HSQ)
2. Pregnancy Drinking Interview & Calendar (PDIC)

Conclusions:
1. The midline CC of young babies (birth through 3 months) can be imaged reliably via careful post-processing of standard clinical ultrasound images by averaged unwarped imaging.
2. A substantial fraction of exposed infants show a potentially diagnostic anomaly of the splenium in these averaged unwarped images.

More information will be provided during the Teratology meetings.

Review of Administrative Cluster – Ed Riley

Administrative Core – Ed Riley

Monthly conference calls with the Steering Committee working very well.
Individual components expected to produce more as a group than individually.
We have to establish common rules regarding testing procedures.
At meeting in January, we redefined organization into clusters and reduced the size of Steering Committee.
Established a website, still need input.
Website address: www.sci.sdsu.edu/CIFASD/ - includes tests, minutes of meetings, manuals, project and PI information.
Joe Jacobson is currently investigating Certificate of Confidentiality rights.
Funded Claire Coles and Tina Chambers travel to Moscow.
Still to be accomplished:
Complete Certificate of Confidentiality
Get Science Advisory Board appointed.
Finish and vote on Statement of Authorship and Rights.
Evaluate projects after 1 year period.
Draft CIFASD Publications Policy.
Need to decide if PIs are to be included on vote or only to include Steering Committee members.
Regarding Teleconferencing:
One site has to be designated as the lead site.
Beneficial for sites overseas (visual images are a problem).
To be used for demo purposes as well.

Informatics Core – Craig Stewart

There have been several personnel matters impacting progress of the Informatics Core in the past year. These issues have been addressed.
Cristina Deximo has been hired as a database programmer and will dedicate 60% to the Informatics Core (100% until the Informatics Core is caught up with all work planned for years one and two).
Stewart's responsibilities will be returning to the state expected at the time the grant was written.
The budget has been modified, essentially decreasing the charges to the grant for systems administrators and management, and increasing the programmer effort.
Specific Aim #1: The Informatics Core will work with CIFASD units to create & disseminate a common data dictionary for data shared within the consortium.
Specific Aim #2: The Informatics Core will advise and consult with each of the other CIFASD participating units so that the data storage mechanisms within each participating unit and facilitate data transmission to the CIFASD Data Repository. The Core will create a manual for the submission of such data.
Specific Aim #3.1: The Informatics Core will provide consulting on experimental designs and analysis and ensure that the data are analyzed and scaled in a fashion that makes possible comparisons across the research programs, cores and pilot studies.
Specific Aim #4: The Informatics Core will provide quarterly summaries of data held in the CIFASD Data Repository, including summaries of new data submitted during the quarter. The first such summary will be disseminated between the 1st and the 15th of October, 2004. Reports will be prepared as requested.
Website: CIFASD_IC@INDIANA.EDU
Andy Arenson is continuing to do heavier aspects of work for project.

Data repositories: once they are in the "data dictionary", it will become standardized. This was agreed upon by scientific directors.

Review of Behavior/Brain Cluster

Neurobehavioral Core – Sarah Mattson, Ed Riley

Testing Materials:
All materials were ordered & distributed to sites.
Communication maintained with PIs as the battery changed and there were some glitches in obtaining the tests.
Equipment:
Decisions were made regarding best equipment, i.e., joysticks, etc.
Translation:
We were able to obtain these forms for free for ASEBA.
Research done as to which letters would be best used for translations.
Translations requested for various phrases needed for computerized tests.
Scripts generated as soon as possible – it is read to you by the computer.
Morris Water Maze done.
Administrative Manual:
To reflect standardized procedures.
Updated based on pilot testing in San Diego and input from PIs/consultants/test authors (in progress).
Test Packet created; used to collect data (Claire Coles did DVD of lighter).
Troubleshooting:
As questions or problems come up.
More on Standardized Administration:
Scoring manual, test and video are being generated with goal of clear and standardized administrative data collection and scoring across the various sites.
Neurobehavioral Core test children 7-18 years of age.
Consult to Informatics Core: Problems
a) ID #s, b) technical problems, c) manuals still need translations, d) exposure/demographic variables need to be identified, and e) retrospective and prospective.
Currently:
May/June: CBT psychometrist
June: testing of real subjects
July: training of Finnish and Russia personnel.

Brain Imaging Core

Review of Individual Projects

Risk Factors in FASD in Moscow Region – Christina Chambers

Cohort study in Moscow Region progress October-December, 2003 includes Jones, Keen, Hull and Chambers.
We hired a native Russian-speaking program assistant/physician on the US side.
Made final year 1 visit of study team to Moscow – training on Bayley for 3 testers @ 6 months to 2 of 4 hospital sites.
Equipment:

- Bayley kit (developmental test)
- 1 digital video camera
- 4 digital cameras
- Digital recording equipment for ultra sound scans (at only 1 hospital site).

We have been functioning with no funds.
Recruitment to begin in August, 2004.
New Features:
Reduced indirect costs as UCSD subcontract for Ukraine project. Need additional 10K for UCSD for CDT testing.
Additional needs for further support from neuropsych core in year 2 for training and support.
In process of accessing ability to use common data; end result will be questionnaire.

Cross Cultural Comparison of FASD – Sarah Mattson

Specific Aims:

To determine whether a phenotype exists in children with fetal alcohol spectrum disorders (FASD). This aim is being addressed by study of three populations of children with FASD in the United States (San Diego), Russia (Moscow), and Finland (Helsinki). The third site (Helsinki) was added as a subcontract to this award after the initial application was submitted. The project includes neuropsychological assessment (all sites), dysmorphological evaluation (all sites), 3-D facial imaging (all sites), and brain imaging (SD and Helsinki).

Studies/Results:

- We have identified and hired personnel at both the San Diego and Moscow sites.
- IRB: We have obtained IRB approval for all sites
- For the Finnish subcontract, the contracts are in place. For the Moscow component, we have requested that funding will be administered through the CRDF and are awaiting approval.
- We have obtained all testing materials and computers to administer tests. Most of the computerized tests are operational; the remaining ones will be complete shortly.
- Pilot testing has been conducted at the San Diego site. This served to streamline the test battery and troubleshoot the administration procedures.
- Data collection has begun in San Diego and Finland (see description of subcontract progress below). The Moscow site will begin data collection in September.

Training-phase I (Coles): In May, Dr. Claire Coles traveled to Moscow for a separate component of the consortium project and was able to conduct some preliminary training on the materials to be used for this project.

Training-phase II (Mattson): During the first week in July, key personnel from the Finnish site and the Moscow site traveled to San Diego (following the RSA meeting) and participated in extensive training on the methods required for the project. Great progress was made toward uniform data collection.

Plans:

During the next funding period, we anticipate completing neuropsychological examinations on approximately 20 children in San Diego and 50 children in Moscow using the neurobehavioral core tests and beginning the planning and execution of our site-specific measures of interhemispheric interaction. We also hope to conduct dysmorphological and 3-D facial imaging studies on these same children this year as well as begin our brain imaging studies. In Finland, the plan is to continue the dysmorphology and 3-D facial imaging examinations and begin the neuropsychological examinations.

Finland Project – Ase Fagerlund

Specific Aim #1 – evaluate long term outcome for FASD in adolescence.

Specific Aim #2 – assess the neurocognitive profile of FASD subjects.

Specific Aim #3 – obtain further understanding concerning the neurobiological pathology and structural abnormalities using MRI and MRS.

Personnel on project: Ilona Autti-Ramo, PI; Marit Korkman, Co-PI; Ase Fagerlund, Project Coordinator; Nina Ervalahti, Assistant; Leena Loimu, Nurse. In process of gathering FASD patients, telephone interviews, MRS studies, and dysmorphology.

Approximately 70 children and young adults with a preliminary diagnosis of FAS/FAE (age range 8-20) from clinical patient pool at the University of Helsinki. Cigarette smoking during pregnancy is very common. Other substance abuse (cannabis, heroin, amphetamine, etc) during pregnancy very rare in Finland before late 90s – FASD group with very few mixed prenatal substance exposure. Significantly more girls (58%) than boys (42%) – mean age 13. By June 18, 2004, a total of 43 patients evaluated by Eugene Hoyme.

Patient Evaluations – family, pregnancy, birth, medical, developmental and histories and dysmorphology exams. Information gathered via review of patient records and interviews of foster families.
Implemented consortium dysmorphology core scoring sheet.
Plans for remainder of 2004:

- Neuropsychological testing – FASD group.
- Teacher reports.
- 3-D Cameras.

Plans for 2005:
Examine control/contrast groups (n=60-70).

- Neuropsychological-testing
- Material interviews
- Teacher Reports
- Dysmorphology evaluations

Neuroimaging
Volumetric MRI
MEG
(fMRS)
(fMRI)

International Neuropsychological Study of FASD – Colleen Adnams
Background:
Designed effective treatment requires specification of core & peripheral deficits.
Lack of access to large groups of well-diagnosed children with FAS/FASD has prevented designed of outcome studies that employ rigorous scientific methodology.
Minimal exchange of ideas among educators, clinicians and basic scientists with regard to development of effective intervention programs.
Broad goal is to examine effectiveness of cognitive and behavioral interventions in a well-defined cohort.
Study will benefit from the neuropsych study, but also contribute to data on the cognitive profile of children with FASD.
Interventions aimed at certain deficits may effect improvements in other deficits, thus helping to identify primary (core) and secondary deficits.
Specific Aims:
Cognitive control therapy
Linguistic and literary training
Family intervention
Recruited Professional Resources: a psychometrist and a coordinator.
Methodology:
80% grade participants at 10 schools from Wellington, 3 epidemiology study, (extensive demographics data).
65 FAS/PFAS: 15 'deferred' on initial diagnosis; confirmed exposure to alcohol.
Randomized to 3 interventions and 1 control group.
Baseline assessment is: 18 month intervention (school months-2years), mid, post intervention assessment.
Analysis focuses on clinically, statistically significant improvements and scale of change.
Progress:
Approvals:
IRB: UNM, UCT
Dept of Ed (PGWG)
Contract in process (UNM & UCT)
Currently in negotiations and planning with schools.
We have a secured research site.

Intervention Study in South Africa – P. Kodituwakku
Specific Aims:

1. To administer a neurobehavioral core test battery to children with confirmed prenatal alcohol exposure from a community in South Africa and on a number of American Indian reservations in the U.S. The data gathered through this test battery will be eventually being combined with those collected at other international research sites.
2. To test a specific statistical model of neurocognitive functioning (e.g., radex model) in children with prenatal alcohol exposure. Radex or hierarchical models of cognitive abilities posit that complex tasks that are at the top of the hierarchy load on what is known as general or 'g' factor. We hypothesize that those complex tests at the top of the hierarchy highly discriminate between children with substantial prenatal alcohol exposure and normal controls.

Personnel: Hired an educational psychologist and a project coordinator, both of whom are Afrikaans speaking.

Community Preparation & Training:

- Visited South Africa in March and met with some school principals.
- Trained the test administrator in some tests that will be used.

Plan:

- July-August: Test manual will be translated and additional training will be provided to the test administrator.
- September: Data collection begins.

Northern Plains:

- Approval from tribal councils is being sought.
- Training the postdoctoral fellow in test administration (July-August).
- Projected beginning of data collection – fall, 2004.

Found that although autistic children have a very high IQ, they are experiencing difficulty with the test.

Identification of FASD in South African Children – Sandra Jacobson

Aims:

- To administer new tests of arithmetic and executive function based on contemporary models derived from event-related potential and neuroimaging studies, in order to improve identification of core deficits of FAST.
- To investigate degree to which deficits in eye blink conditioning found in animal studies can be detected in children heavily exposed to alcohol.
- To test hypothesis that two moderator variables – maternal age and the absence of an ADH2*2 allele – can improve identification of FASD in prenatally-exposed children.
- To evaluate usefulness of Fagan test, infant numerosity and A-not-B for early diagnosis of FASD by assessing their predictive validity in relation to specific elements of arithmetic and executive function found to be associated with prenatal exposure during early childhood.
- To determine degree to which photographs taken using a new 3-D camera may make it possible to detect differences among FAS, ARND, and controls and improve validity of FASD diagnosis by detecting subtle craniofacial anomalies in children with ARND.
- To administer cognitive and behavioral assessments from CIFASD Neurobehavioral Core that are relevant for this age to provide data on neurobehavioral sequelae of FASD that can be pooled and compared across age, site, and ethnic group.

In the US:

- Sandy and Joe met with Mark Stanton to review EBC data collected on first children in cohort.
- EBC data look very good so far – all children were conditioned in the short delay condition.
- Consulted regarding two innovative preschool number processing assessments recommended by Stan Dehaene.
- Waiting to add NES-3 CPT test and Virtual Water Maze.

- Set up Teleform, which permits data to be scanned directly from data collection forms into computer Bullet 2.

Progress to date:

- Testing of cohort began on May 17, 2004.
- To date, 6 children and their mothers have completed the 2-day visit to the lab.
- Children comfortable with and generally enjoy assessments.
- EBC data are transmitted via email to Detroit for analysis.
- Stressed that lack of communication is a big issue.
- Sub-committees should be formed to decide on Informatics Core questions.
- Each site is responsible for setting up own data entry.
- Progress is steady and positive.

Overview of Basic Science Cluster – Michael Charness

Review of Basic Science Projects

Rationale for Basic Science component of CIFASD

- Inform clinical studies with basic molecular and animal data on FASD conditioned eyeblink response
- Biomarkers of risk for FASD (5-HT, polymorphisms of kinases, etc)
- Developmental findings
- Development of agents that might prevent FASD in mothers who continue to drink.
- Clearer understanding of pathophysiology may produce more targeted treatments.

FAS Resemble CRASH Syndrome

- Mental Retardation
- Corpus Callosum
- Hypoplasia
- Hydrocephalus
- Cerebellar Dysplasia (vermian lobules 1-5)

Ethanol inhibits cell adhesion in L1-transfected mouse L cells.

Octanol decreases ethanol-induced cell death in mouse whole embryo culture.

- Octanol antagonizes ethanol teratogenicity in mouse whole embryo culture

NAP & SAL prevent alcohol-induced fetal death and growth abnormalities.

Photolabeling of Alcohol Binding Sites on L1 – Keith Miller

Principles of Photolabeling:

- Immediate objectives
- Longer term objectives

SAL treated in prenatal model.

Specific aim #1 – Plan

- Counting brainstems for serotonin.
- NAP treatment in prenatal model.

Specific aims #2

- Identify neuroprotective and neurotrophic effect of NAP/SAL on alcohol induced apoptosis.

Testing of FAS Therapeutic Agents in Neonatal Rodents – Charles Goodlett

Translational basic science for the consortium.

Re: Molecular interventions: How can we protect and what types of functional protection?

Push limits of animal models.

Determining compounds for an interventional tool.

Aim #1 – To test molecular agents.

Aim #2 – To test against long-term deficits.

Aim #3 – To develop eyeblink conditioning procedures in C573L/6J.

Shows alcohol damage during neonatal period – vitamin E supplements does not protect as we thought it would (40-50% affects cells).
Hippocampal – dependent – conditional discrimination eyeblink task
Neonatal treatments in mice to begin in July, 2004.
Neonatal ethanol treatments in rats were piloted and outcomes were glorious.
Trace eyeblink conditioning reveals profound deficits in adult rats treated with alcohol during the prenatal period.

Review of Budgets for Upcoming Year
Renewals due July 1, 2004.

Review of Publications Statement
Authorship issues: information will go out within a week.

New Business
It was suggested that when there is a conference call meetings, that all PIs are would be welcome to participate.
It was decided to expand steering committee to include all PIs. Committee will now be called the Executive Committee.
Craig Steward looking into use of an "800" number through Indiana University can be used for conference calls at a much lesser expense, making it possible for PIs to call in to conference calls, if desired.
Craig will also check into the possibility of having IU purchase a camera then re-sells it back to SDSU Foundation within 3 months. At that time, funds will be available.
Michael Charness will look into camera used at Harvard that doesn't cost $20,000, with reader on site.
Neurobehavioral Core testing should be available to begin fall, 2004.
Document to sell 3-D camera for Phil's usage to present to establishments in Italy.
Ed Riley stressed the need for training, testing reliability and assessments; currently there is no money for these – he is open for discussion/suggestions.
The questions was posed as to which was more important – training or testing?
Also, we need to train individuals to use 3-D camera in Russia and San Diego.
Discontinue collecting data until we are all uniform and on the same page – approximately 1 month.
Dysmorphology – won't change much.
Manual – ready to go to Andy Arenson in 1 month.
Neurobehavioral
Monetary issue
Momentum issue

Closing Remarks
Sub-committee meeting held after CIFASD meeting, June 24, 2004 (Informatics Core – Joe & Sandy Jacobson, Tina Chambers, Andy Arenson, Ann Streissguth). They created a questionnaire re: drinking measures, uniform collecting info.
Ed Riley: Within a month, general information from Informatics will go out for everyone to review.
Michael Charness stressed the need of cross validation of data. Consortium will need to address or answer to the issue that data was not collected differently or go with less data in a uniform (agreed upon) manner.
Phil May added that the information agreed upon from the previous day's meeting is more than sufficient to take us forward. Collected materials from 3 or 4 years ago are consistent with the current questionnaire.
Michael Charness: Concerned about PASS.
Sandy Jacobson: Add comments to information received back from Andy Arenson.
Phil May: Operative word is "recommended" to parents. All need to be applied in a socially appropriate way or you will get false answers or less info.

Next meeting: Scheduled to be held in January, 2005 in San Diego, CA.

Adjournment @ 4:30 pm, June 25, 2004.