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June 17, 2008

Dr. Michael J. Meaney
Douglas Hospital Research Centre
Perry Pavilion

Subject : **Protocol 03/45** *Maternal Adversity, Vulnerability and Neuro-development (MAVAN)*
Amendment – Addition of a visit (60 month interview)

Dear Dr. Meaney,

We acknowledge receipt of the protocol amendment you submitted for approval for the above mentioned protocol. I have examined this request and as Chairperson I give expedited approval to the proposed amendment since it is satisfactory and it meets REB requirements.

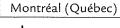Sincerely yours,

for :

Serge Gauthier, M.D., F.R.C.P.(c)
Chairperson
Douglas Institute Research Ethics Board
/gl

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May 28th, 2008

Serge Gauthier, M.D., F.R.C.P(c)
Chairperson
Douglas Hospital Research Ethics Board

Subject: Protocol 03/45 "*Maternal Adversity, Vulnerability and Neuro-development (MAVAN)*"

This letter concerns the protocol 03/45 "Maternal Adversity, Vulnerability and Neuro-development (MAVAN)" which was approved be the Douglas hospital ERB committee on March 15th 2004. We are writing to request approval to add one visit to the current protocol of this study. Please find the rationale and protocols attached.

Thank you and the Committee for your time and consideration.

Sincerely,

Michael J Meaney
James McGill Professor of Medicine
Departments of Psychiatry and Neurology & Neurosurgery
McGill University
And
Associate Director, Research
Douglas Hospital Research Center

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The amendment involves one point: **Adding an evaluation at 60 months**

Summary

Our current research protocol investigates the influence of the early environment on infants' neuropsychological development. Our study is comprehensive and includes variety of psychological and physiological measures. Maternal adversity during **fetal life** including maternal stress (as well as depression), low social support, poor maternal nutrition, tobacco/alcohol consumption predict both preterm labour and intrauterine growth restriction. These birth outcomes, in turn, represent major epidemiological risk factors for neurodevelopmental impairments in children as well as heart disease, diabetes and depression in adulthood. **Postnatal** maternal adversity compromises maternal care/behaviour and infant development. It also predicts increased risk for obesity, heart disease, attention deficit disorders (ADD), drug abuse and depression. Despite the enormous potential for the interaction of prenatal and postnatal influences, research has largely been restricted to the effects of events occurring during only one period in development which, among other things, ignores the potential importance of 'protective' factors operating at later stages in development. Moreover, the underlying mechanisms by which perinatal adversity might directly affect neurocognitive development have been very poorly studied.

The original ethics approval supported the establishment of the MAVAN project as a longitudinal study of high-risk children until 48 month of age. In this amendment, we request the Douglas ERB to extend the project with children of 60 months of age. This will permit the prospective study of gene x environment interaction defining neurodevelopment in children with diagnosable ADD or anxiety disorders. The additional procedures in the MAVAN study were developed with the experience gained with our first cohort, limiting the burden on participants as much as possible. We maintain the same focus with the evaluation of the development of attentional process, with new tests adapted for the 60-month children. Moreover, after 4 years of testing, we know that mothers enjoy the opportunity to have someone visiting them who has an interest in how they and their children are doing. This insight has an empirical base through a questionnaire completed by the mothers in our study identifying the aspects of the MAVAN project considered as positive or problematic. Research assistants have developed a close relationship with mothers and both enjoy the opportunity to meet and follow the evolution of children development.

Justification

<u>Sixty month interview:</u> **First home visit (90 minutes)**

Mothers

Interview: Questionnaire on Maternal Well-Being (30 minutes)

This questionnaire has already been accepted by the Douglas Hospital Ethic Board with the original submission of the MAVAN project. This program of research examines the impact of maternal adversity on child development. Therefore, it is critical that we regularly monitor the level of maternal adversity. An extensive maternal interview protocol was administered at 6, 12, 24, 36 and 48 months post-partum. At 60 months, we plan to administer the same version as used at 24 month.

Questionnaires (30 minutes)

BECK: The **Beck Depression Inventory (BDI, BDI-II)**, created by Dr. Aaron T. Beck, is a 21-question multiple-choice self-report inventory that is one of the most widely used instruments for measuring the severity of depression. The most current version of the questionnaire is designed for individuals aged 13 and over and is composed of items relating to depression symptoms such as hopelessness and irritability, cognitions such as guilt or feelings of being punished, as well as physical symptoms such as fatigue, weight loss, and lack of interest in sex (15 minutes).

Children

Theory of mind:

<u>Forty-eight month home interview</u>: **Second visit (80 minutes)**

Mothers

Questionnaires (20 minutes)

DEBQ (Deutch Eating Behavior questionnaire), Sensitivity to Reward and Punishment Questionnaire, The Seasonal Pattern Assessment Questionnaire (SPAQ)
There is a growing acceptance that overeating of highly palatable foods is a major contributor to the epidemic of obesity occurring in children and adults alike. Emerging work in adults suggests that brain pathways related to addictions are involved in this vulnerability, and that many individuals consume certain foods to alter short term mood states, similar to other drugs. Questionnaires assessing Sensitivity to Reward (Sensitivity to Reward and Punishment Questionnaire) and various aspects of Eating Behaviour (DEBQ: Deutch Eating Behavior Questionnaire) are thus becoming important tools for the identification of individuals at risk for overeating and obesity. About 75% of people with seasonal mood problems report cravings for highly palatable foods, and are an excellent focus for work of thus type. The Seasonal Pattern Assessment Questionnaire (SPAQ) is a brief self-report scale that will be used to screen for seasonal changes in both mood and eating behaviour" (15 minutes).

The following questionnaires have already been accepted by the Douglas Hospital Ethic Board for different time points included in the initial submission. The first questionnaire evaluate family **Housing conditions** (10 minutes) and the **CAQ (Childbearing Attitude Questionnaire)** assesses thoughts and feelings about having a child (5 minutes).

Actiwatch
This measure has already been accepted by the Douglas Hospital Ethic Board for different time points included in the initial submission. We will ask mothers to place a small watch-like device on their child's wrist. The watch is sensitive to movement and measures the quality of the children's sleep. The watch will be placed on the child's wrist for the appropriate period (night time) for 8 consecutive days. We will also ask mothers to complete a short sleep log during that week to inform on the child's bed time and wake up time.

Children

School Readiness Test Battery (60 minutes)

The 'school readiness' test battery predict performance in early elementary school. This measure has already been accepted by the Douglas Hospital Ethic Board for the 48 month assessment. We whish to repeat this test in order to follow the influence of school preparation on later school performance.

Computerized Continuous Performance Tasks (K-CPT) (10 minutes)

This measure has already been accepted by the Douglas Hospital Ethic Board for the 48 month assessment.

Sixty month interview: Laboratory visit (120 minutes)

Mothers

Computerized tasks (60 minutes): *The following tasks will be filled while children perform the CANTAB tasks*

The assessment of the mothers includes an abbreviated version of the health and well-being interview protocol the mothers have received in previous years. In addition, this year the mothers will do two sets of computer tasks while their child is being assessed at the lab visit. The two computer tasks are social cognitive measures designed to assess implicit attitudes about self, romantic partner and child. Increasingly research has revealed that human behavior often operates automatically and not always in a consciously controlled manner. Whereas questionnaires often elicit controlled and deliberate responses, implicit measures assess quick, reflexive cognitive associations that predict automatic behaviors. This is especially important to assess for mothers in the context of very busy, demanding daily life. When people are busy, tired, or distracted, they are most likely to behave toward others such as their child in an automatic, non-deliberative way, based on their implicit attitudes more than their explicit (self-reported) attitudes.

The first task is the Implicit Association Test (IAT) and aimed to evaluates self esteem. The second task is one of the most common computer task in social and cognitive psychology, the lexical decision task, evaluating attachment style.

Questionnaires (20 minutes)
The following questionnaires have already been accepted by the Douglas Hospital Ethic Board for different time points included in the initial submission. The first questionnaires assess the Health (5 minutes) and Sleep patterns (5 minutes) of children, and the Childhood Behaviour Checklist questionnaire (CBCL) is a well-validated screen for childhood psychopathology.

Children

Koala Fear questionnaire: (5 minutes)
The Koala Fear Questionnaire (KFQ) is a standardized self-report scale for assessing fears and fearfulness in children aged between 4 and 12 years. This scale consists of 31 potentially fear-provoking stimuli and situations that are all illustrated with pictures. Children rate the intensity of their fear of these stimuli by using a visual scale depicting Koala bears expressing various degrees of fear (

no fear, some fear, a lot of fear). The use of pictures and the visual fear scale make the KFQ suitable for younger children. Furthermore, research has indicated that fears in childhood are frequently related to other unpleasant emotions, in particular anxiety (e.g., Ollendick, Yule, & Ollier, 1991). Researchers are increasingly convinced that high levels of fear and fearfulness in pre-school children may be significant predictors of serious anxiety problems in later childhood (e.g., Craske, 1997). (Muris and al., 2003).

Attention Tests: **CANTAB (60 minutes)**
      This measure has already been accepted by the Douglas Hospital Ethic Board for the 48 month assessment. For the 60 mo assessment, we want to add two subtests: "Stocking of Cambridge" and "Delay Matching to Sample". Our selection includes tests that show variation in 4-5 year olds, as well as tests where performance is well below that of adults until the time of puberty. The inclusion of such tests is based on our intent to sustain studies of the MAVAN populations into adolescence and beyond.

New tests included in the CANTAB battery:

1) **Delay Matching to Sample (DMS)** assesses forced choice
   recognition memory for novel non-verbalisable patterns.

2) **Stockings of Cambridge (Tower of London):** SOC assesses spatial
   planning and motor control.

Mother-child interactions (25 minutes)
      After children performed half the attention tasks, they will be allowed to rest with their mothers for a 25 minutes period. For the purpose of observing the parent-child dyad, parents and children are videotaped together for four 5-minutes segments of 1)Feeding, 2)Structured task, 3) Free play, 4)Separation-reunion. Each of the 4 situation provide a window for understanding what has been shared in the parent-child relationship. Each situation is experienced differently with some eliciting conflictual feelings and others allowing for feelings of competence in the parenting role. For coding purposes, we will videotape this session. Children will then continue with the last tasks of the CANTAB.

Impossible puzzle: (20 minutes)
The cognitive-vulnerability model of depression (Beck, 1964) is one approach at the forefront of research in this field. The theory states that people who possess a maladaptive cognitive style (i.e. negative attributions etc.) or *vulnerability* are at greater risk to develop symptoms of depression or depressive disorders. However, the antecedent conditions that determine cognitive vulnerability are not clearly understood. A developmental approach suggests that a child's early environment, including the mother-child relationship fosters maladaptive thought processes. An intriguing study by Cole et al. (2007) examined vulnerability in 95 kindergarten children (mean age X=5.3) to test learned helplessness. To measure child vulnerability they administered an " impossible puzzle-task", where the child participated in seven, two minute puzzles.
      In our version of the puzzle task the children work on a total of five puzzles; the first and last puzzle represented relatively easy, possible tasks, whereas the middle three puzzles are impossible. We created the impossible puzzles by making modifications on selected versions of the *Shape by Shape* puzzles by Binary Arts. Children start by completing a "possible" puzzle. The research assistant then

tells the child that they will have tow minutes to work on each of the rest of the puzzles. Children work on a succession of three (impossible) puzzles. After each puzzle, the research assistant ask the child three questions: (1) How do you think you did on the puzzle? (selfevaluation); (2) how do you think you will do on the next puzzle? (hopefulness); and (3) how do you feel about doing another puzzle (motivation)? For the first two questions, children respond on a laminated star chart by pointing to how many stars out of five they deserve (with one star = not very well; three stars = OK or not bad; five stars = very well). For the third question, rating how they felt about doing another puzzle, children use a different answer board and pointed to one of five faces (e.g. 1 = frowning, 3 = neutral, 5 = smiling). The research assistant then give the child unlimited time to work on a fifth solvable puzzle, and praise the child for its successful completion. The task is videotaped for future coding. (Cole et al 2007; Early Predictors of Helpless Thoughts and Behaviors in Children Developmental Precursors to Depressive Cognitions).