DGIM Project Summary

**Name of Project:** “Neurosteroid Metabolism and the Antidepressant Effects of Serotonin Specific Reuptake Inhibitors (SSRI’s).”

Nickname: “MDD STUDY”. CHR Approval # 10-00825, Approval Expires 01/14/2012

**Investigators:**

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**Research question(s):**

We are seeking to test the following hypotheses.

**PRIMARY HYPOTHESES:**

1. Neuroprotective factors are deficient in depression, and antidepressant treatment stimulates these factors.
2. Depression is a chronic stress syndrome which results in accelerated cellular aging and a higher oxidative stress index.
3. Genetic abnormalities interact with early trauma history to increase the vulnerability to depression.

**SECONDARY HYPOTHESES**

1. Specific memory functions are disturbed in depression, and these are related to deficient neuroprotective factors.
2. Depression is associated with chronic changes in appetitive behavior with resultant physiological and metabolic disturbances

**Brief Background/Significance:**

It has been demonstrated that chronic stress results in a shortening of telomeres. It is possible that major depression, as a form of chronic stress, also results in shortening of telomeres. There may also be interactions between the action of SSRI’s and telomere length, as well as levels of telomerase.

**Inclusion/exclusion criteria (list)**

**INCLUSION CRITERIA**

All participants must meet the following criteria:

- Age 18-70 y.o.; Good general medical health: Clinical labs (electrolytes, liver function test, CBC) with no clinically significant abnormalities; Negative urine toxicology (drugs of abuse) screen; Taking no medication or drugs likely to interfere with the study objectives (including birth control pills), except as allowed by protocol; Free of any antidepressant, mood-stabilizing or anti-anxiety medication for a minimum of 6 weeks before entry into the study (with the exception of prn benzodiazepine, anxiolytic or sedative-hypnotic use, < 3 nights per week); No current diagnosis of PTSD; No history of angina or known coronary artery disease.; Lab results demonstrate an Hct of 36-48 for females and 38-54 for males, or a Hgb of between 12.5-20, for all participants regardless of age.

**Additional criteria for Depressed Participants:**

- Current DSM-IV Axis I diagnosis of Major Depressive Disorder, unipolar, without psychotic features (co-morbid diagnoses of Panic, Generalized Anxiety Disorder, or Phobias are permitted); Baseline 17-item Hamilton Depression Rating Scale (HDRS) rating of > 17; Baseline HDRS item #3 (“suicidality”) rating of ≤ 1, and clinician’s determination of absence of active suicidal intent.; No anticipated changes in psychotherapeutic interventions during the study.

**Additional criteria for Normal Controls:**

- No DSM-IV Axis I diagnoses

**Method of contact/recruitment (be specific)**

We will have an assistant do a STOR search for patients who are diagnosed with depression and who are not currently on antidepressants. We will then send a letter to their primary physician describing the study and expressing our interest in the patient. **Instead of sending one letter per patient, we will send each physician one letter**
inquiring about all of his or her patients that are of interest to us. They physician will have an opportunity to decline on behalf of the patient. Then, we will send a letter to the patient, describing the study and giving them an opportunity to decline participation. Then we will call them and screen them by phone. Then we will invite them for an in-person screening visit. 2. We will also be recruiting participants through ads on Craigslist, and flyers, but those methods do not specifically involve DGIM.

Benefits/burden for participants (clearly identify potential for harm)
1. Sertraline Treatment: We are using sertraline (Zoloft), which is a highly selective SSRI shown to be effective in treatment of major depression. Sertraline is the most commonly prescribed FDA-approved antidepressant in the US. In the doses used in this study, it is considered very safe. We screen out participants with current suicidality, and development of suicidality would be cause for terminating participation and referring the participant to standard clinical care. We follow participants closely, with mandatory clinical evaluations at Baseline and at Weeks 1, 2, 3, 4, and 8 of treatment, plus additional clinical contact as needed. Significant clinical deterioration (judged by the investigators or by the subject) will lead to discontinuation and referral to clinical care.
2. Limitation on Other Treatments: Participants are only eligible to participate in this study if they have not been taking psychotropic medications for six weeks prior to beginning the study, and no new non-study related psychotropic medications may begin during the course of the study. No new courses of psychotherapy may begin during the study.
3. Venipuncture. Standard venipuncture risks are pain, possible infection and fainting. The total amount of blood to be drawn during the Baseline visit and during the Week 8 visit will be approximately 190cc per visit. Thus, the healthy controls have approximately 190 cc of blood drawn, and the depressed participants have approximately 380 cc of blood drawn over an 8-week period.
4. Saliva collection: This is without risk except for the mild inconvenience some participants may experience.
5. 24 hour urine collection: This is without risk except for inconvenience.
6. Dexamethasone Suppression Test: The dexamethasone (up to 0.5 mg.) has no known risks associated with it, because it is a very low dose and single administration of synthetic glucocorticoid.
7. Body measurements: There is no except possible embarrassment.
8. Behavioral ratings: These are generally without risk except for the inconvenience and time required.
9. Genetic Studies: Donating genetic material could result in a loss of confidentiality. We make every effort to preserve the confidentiality of genetic ands well as complete health information.
10. Confidentiality: Participation in research may involve a loss of privacy, but information will be handled as confidentially as possible.
11. MRI: The MR apparatus attracts certain metals so there is the small possibility that magnetic objects will accidentally fly into the magnet. This risk is greater at 4.0 Tesla field strength. Subjects who have metal in their bodies that may interfere with the magnet may not be admitted to the study. This will be determined on a case-by-case basis. Clothing (including undergarments that contain metal) may not be allowed in the 4.0 Tesla MR unit. Instead, we provide subjects with a hospital garment to wear for the MR procedure. NOTE: The MRI is currently removed from our study due to lack of funding, but it may return in the future if and when more funding becomes available.
12. Actigraphy: This may produce slight discomfort from prolonged wear. That is the only known risk.
13. BIA (bioelectric impedance analysis): May involve slight social discomfort. That is the only known risk.

Any benefits or burden to DGIM practitioners?
The possible benefit or burden to DGIM practitioners is minimal. They will receive only one letter from us, which they only need to respond to if they object to us contacting their patient.

Timeline for recruitment (projected start and stop dates)
For our DGIM recruitment, we would like to start sometime in May 2011. Then, we may do it again once every 3-6 months for approximately the next 5 years.

Funding source
NIH: National Institute of Mental Health, Award # A114651

Potential for DGIM collaborators?
At the moment, we are only planning on collaborating with Mitch Feldman and the administrative assistant whom we will hire. However, we are open to collaborating with other DGIM physicians (and residents) if they have an interest.

Do you agree to notify us when recruitment is completed? Yes.

Date form completed:
Form completed 04/18/11 by John Coetzee. Updated 07/10/11 by John Coetzee.