**Proposal Cover Sheet**

**Term: Fall 2011**

**Instructor: Nora Demers**

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Present Year in Education: Senior

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Major: Biotechnology

Have you identified a research mentor for a senior thesis (if applicable)?

\_\_\_\_\_ Yes \_\_X\_\_ No.

If yes, please identify.

Name: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**Title of Proposal:**

**Use of Intranasal Oxytocin as Treatment in Young People with Autism Spectrum Disorders by Improving Social Communication**

Keywords (3-5): Oxytocin, Autism, Facial Recognition, Treatment

**Checklist:**

All required portions of the first submission are included \_\_\_\_\_ Yes \_\_\_\_\_ No

I had an external reviewer read the proposal \_\_\_\_ Yes \_\_\_\_\_ No

If Yes, who \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ When \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

I authorize the use of this proposal as an example in future courses \_\_\_\_\_ Yes \_X\_ No

**Abstract:**

Individuals with autism have impaired social functioning. Recently it has been suggested that intranasal oxytocin may play a role in increasing social recognition among children with autism spectrum disorders through increased gaze time at the eye region of others. Our study will have 34 male participants with varying profiles of autism. We will administer each patient an intranasal oxytocin solution followed by a placebo spray one week apart and regulate progress with the Reading the Mind in the Eyes Test Revised to see if there is a difference between the two sprays, indicating an increase in social recognition.

**Table of Contents**

Page

I. Abstract 2

II. Project Description 4

a. Introduction 4

b. Research Objectives 5

c. Methods 5

d. Broader Implications 7

e. Timetable and Project Management 8

III. References Cited 9

IV. Curriculum Vitae 11

V. Special Materials 13

**Project Description:**

**Introduction:**

Autism is a developmental disorder characterized by abnormalities in speech and communication, impaired social functioning, and repetitive behaviors and restricted interests. It is the prototype disorder of social dysfunction (APA, 2000). One of the key impairments is an inability to respond appropriately to social cues, including failure to accurately interpret facial expressions (APA, 2000). Face-processing and emotion recognition impairments have been confirmed by cognitive, behavioral, and neuroimaging studies, across both auditory and visual sensory modalities (Baron-Cohen et al, 2000). These are specific impairments related to social cognition, which are likely to be heritable (Losh et al, 2009). They are believed to play a key role in the failure to acquire social skills across developmental stages (Klin et al, 2002).

Advances in social neuroscience have identified the neuropeptide oxytocin as playing a key role in social behavior (Donaldson, Young, 2008). Oxytocin anomalies have been reported in children with autism. Oxytocin is a nine-amino-acid peptide (nonapeptide) that is synthesized in the paraventricular and supraoptic nucleus of the hypothalamus and released into the bloodstream by way of axon terminals in the posterior pituitary. In addition to its release in systemic circulation, oxytocin is widely distributed throughout the central nervous system, and there are prominent oxytocin receptor binding sites, especially throughout the limbic system (Insel and Young, 2000). This ancient mammalian peptide enhances peer recognition, social approach, and bonding behavior across numerous species (Donaldson, Young, 2008). In typical healthy humans, oxytocin nasal administration improves emotion recognition (Domes et al, 2007) and face processing (Guastella, Mitchell, Mathews, 2008). This has led some to speculate its use for the treatment of psychiatric disorders characterized by social deficit (Donaldson, Young, 2008; Guastella et al, 2010). Children with autism have significantly lower plasma oxytocin levels compared to control subjects (Modahl et al, 1998) and fail to show the normal developmental increase in oxytocin blood levels. Plasma samples are associated with higher oxytocin precursor levels, suggesting that autism may be related to anomalies in the way this hormone is synthesized (Green et al, 2001; Andari et al, 2010). Recently, it has been shown that oxytocin facilitates recognition of memorized faces and strengthens the encoding of social stimuli (Guastella, Mitchell Mathews, 2008; Savaskan et al, 2008). Moreover, oxytocin has been reported to increase the time spent looking at socially important cues, such as the eyes, when viewing pictures of human faces (Guastella, Mitchell, Dadds, 2008).

**Research Objective:**

This study will investigate the effect of oxytocin in children with varying profiles of autism spectrum disorders on their ability to communicate in social settings. A study by (Guastella et al, 2010) has been done examining the effect of oxytocin nasal spray in a small group of young patients with high-functioning autism spectrum disorders. This study found that there is improvement in autistic patients who had been administered oxytocin. Testing a larger sample size with various autistic profiles and ages will provide greater insight into the degree to which oxytocin increases social recognition and social communication in children with autism spectrum disorders.

**Methods:**

Using the methods of (Guastella et al, 2010), at initial contact, all participants will be screened for a significant degree of autism symptomatology using the parent version of the Developmental Behavior Checklist; which is a descriptive-empirical approach to individual symptoms, and a measure of the properties of a symptom list. The advantage of such an approach is considered to be that it makes no assumptions about the nature or taxonomy of psychopathology in children and adolescents with mental retardation (Einfeld, Tonge, 1995). For this study we will recruit 34 male subjects aged between 10 and 21 years who are diagnosed of Autistic Disorder or Asperger's Disorder (APA, 2000). Participants will be recruited between December 2011 and March 2012 through local advertisement. In a double-blind, crossover, and randomized controlled trial, participants will be assigned to receive a single dose of oxytocin and a placebo nasal spray one week apart (Guastella et al, 2010). Seven participants will be selected from each of the four IQ groups (Mild, Moderate, Severe, and Profound Retardation) of autism screening scores to progress further. Six participants will be from an unknown IQ group. Participants will then provide evidence of a documented mental age of 8 or greater as indicated by cognitive assessments conducted within the past 3 years. In the absence of previous testing, participants will be assessed by a neuropsychologist using the age-appropriate Wechsler Intelligence Scale (Wechsler, 1997). Participants will complete a medical and psychiatric review with the study psychiatrist (S.L.E.) to confirm diagnosis using both Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) assessment criteria and case review. This assessment will classify the individual as having an autism spectrum disorder. These will be additionally reviewed by a multidisciplinary team. Exclusion criteria included females and known allergy to preservatives contained in the nasal spray (viz., E216, E218, and chlorobutanol hemihydrate). Participants will be instructed to abstain from alcohol and caffeine on the day of drug administration and food and drink (except water) 2 hours before drug administration. A description of the study and written consent will be obtained from participants and permission must be granted by the IRB. Consent will also be obtained from parents or caregivers if participants are under the age of 18. Participants will be told they can withdraw at any time (Guastella et al, 2010).

Nasal sprays will be synthesized by a compounding chemist (each puff per nostril contained three international units [IU]), with an identical placebo containing all ingredients except the active oxytocin. The older age group of participants (aged 16–21) will receive a dose of 24 IU (4 puffs per nostril), which has been selected for most adult oxytocin nasal spray research studies. Those aged 10 to 15 years will receive a 75% dose of 18 IU (*n* = 11, 3 puffs per nostril) (Domes et al, 2007; Guastella et al, 2008). Participants will complete side effect reports upon completion of each experimental session.

Based on previous oxytocin and related peptide nasal spray research (Domes et.al,2007; Guastella et al, 2008; Born et al, 2002), we will present the Reading the Mind in the Eyes Test-Revised (RMET) (Baron-Cohen et al, 2001) 45 minutes following drug administration to assess the effects of oxytocin on social recognition. This test assesses one's ability to read emotions from the eyes of affective facial expressions, through a series of photos of the eye region, and is the most widely used test of emotion recognition in patients with autism, (Haxby et al, 2002; Baron-Cohen, 2001). We confirmed that the test had been previously used in high-functioning autism samples aged as young as 12 (Golan, 2008). It measures how well a patient can read facial expressions by focusing on the area of the face around the eye. These data sets will be analyzed using a Mann Whitney U-test which compares the calculated Umin to a critical U-value, to see if the data sets are significantly different. U is calculated by the equation where R is the sum of the first group of values and n is the sample size. U will be calculated for both data sets and the smaller of the two U values will be the Umin.

**Broader Implications:**

This study could heighten social behaviors in young children when functional development is most probable (Guastella et al, 2010). By finding supportive evidence of oxytocin as treatment for young people with autism spectrum disorders, we will be able to provide a better standard of life by allowing them to interact with other individuals on a higher level.

**Time Table and Project Management:**

Possible participants in the study will be interviewed from December 2011 until May 2012. From the interviewees we will select those who will partake in our study. Written consent will need to be collected by the chosen participants, and parental consent for those under eighteen, no later than June 15, 2012. Each participant will also need to verify their mental age by this date, based on a cognitive test taken within the past three years. Each participant will complete a medical and psychiatric review with the study psychiatrist (S.L.E.) to confirm diagnosis using both DSM-IV assessment criteria and case review by the last day of June 2012. On the seventh day of July we will give six of the participants the oxytocin nasal spray and record their results from the Reading the Mind in the Eyes Test Revised. This will continue until July 12, 2012 with six new participants each day, except for the last day when only four participants will be tested. On July 14, 2012 the first group of participants will return to receive the placebo and again will be tested using the RMET and their results will be recorded. This will continue until July 19, 2012 when the last group of participants will be tested with the placebo. Results will be obtained within the next month. A psychiatrist will need to be hired to perform the pre-study DSM-IV assessment criteria. One person will be able to perform the following duties assigned over the time frame given.

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**GOALS**

After obtaining my Bachelor’s of Science degree for Biotechnology I will be pursuing a medical related career path, specializing in neurology.

**EDUCATION**

BS: Florida Gulf Coast University, 2012, Biotechnology

Minors: Biology and Chemistry

High School: Galena High School, 2008, General Studies

Courses:

Cell Biology

Genetics

Organic Chemistry

Biochemistry

Microbiology

**EMPLOYMENT**

Research/ Medical/ Pharmaceutical Employment:

CVS Pharmacy: Cashier, February 2010-April 2011

**PROFESSIONAL SOCIETIES**

Phi Eta Sigma National Honor Society, inducted spring 2009

**SERVICE**

Volunteer:

HealthPark Hospital, will be helping with patients, November 2011-May 2012

AYSO Soccer Coach, 4-5 year old age group, April 2011-August 2011

Academic service:

Phi Eta Sigma Relay for Life, 2010

Community outreach:

Elks Christmas Basket Delivery, December 2007-present

**AWARDS**

Academic:

President’s List, Fall 2008

Dean’s List, Spring 2009

**SCIENTIFIC SKILLS**

Gel Filtration Chromatography

IR Spectroscopy

NMR Spectroscopy

Gram Stain

Culturing Cells

**Expected Equipment and Special Resources:**

To conduct research the following materials are required:

1. Psychiatrist to perform DSM-IV assessment
2. Oxytocin will be synthesized by a compounding chemist
3. Reading the Mind in the Eyes Test Revised pictures; internet access
4. Expected Cost:
5. Psychiatrist: $64/hr for 34 hours; $2167
6. Oxytocin and Placebo: $15 for 68; $1020
7. Compounding Chemist: $500
8. Participants: $10/hr for 64 hours (2 hours per participant); $640
9. Total Funding Required: $4327