Appraising Animal Models of Autism: Toward a Meta Analysis

Author: Laura Sang (3rd Year Undergraduate Student, Interdisciplinary School of Health Science)
Supervisors: Katie Greig (B.A. Candidate, School of Psychology) and Anne TM Konkle, Ph.D. (Assistant Professor, Interdisciplinary School of Health Sciences)

Developmental Neuroendotoxicology Lab

uOttawa
L'Université canadienne
Canada's university

ABSTRACT

Autism spectrum disorders are a subcategory of neurodevelopmental disorders characterized by stereotyped and self-injurious behaviours as well as impairment in social interactions and communication (Geier 209). The onset of symptoms often occurs in early childhood and is 4 times more predominant in males (NIHM (b)). The cause of the sexual dimorphism associated with autism is still unknown, despite years of scrutiny on the part of the scientific community. My project was to assist a 4th year Honour's student examine current animal models of autism and help extrapolate data that may provide clues into the causal mechanisms of the aforementioned sexual dimorphism. All selected articles maintained a focus on the modification of behaviour resulting from autism spectrum disorders, as well as the observed effects on various brain areas including, but not limited to: the frontal cortex, the hippocampus, and the cerebellum. A pool of articles was formed and the articles were coded using a guide (developed by the Honour's student). After coding , the data was entered into a computer program that would aid with a meta-analysis. Results are currently pending. From the act of coding, I observed that rodent exposure to valproic acid and pathogens can lead to DNA alteration, widespread changes in neurotransmitter concentration in several brain areas, and behavioural deficits occur that closely resemble the symptoms in humans.

INTRODUCTION

- ⬆ Autism and related disorders over the past century
- 3.4/1000 children (ages 3-10) are afflicted (NIMH (a),(b))
- 4:1 ♂ : ♀
- ♀⬆ cognitive impairment and more severe symptoms (NIMH (a))
- Potential causes: genetic, environmental or viral origins (prenatal viral infection, brooks)
- Symptoms: in toddlers – abrupt personality change, becoming aloof, antisocial and potentially self-abusive (NIMH (a))

GOAL: gain a better understanding of the etiology behind this sexual dimorphism by examining the current animal models of autism. The effectiveness of the methods in inducing autistic symptomatology will be assessed via meta-analysis.

Animal models :
•Beneficial because they have similar neurobiological pathways
•Rodents reproduce more frequently than humans

METHODS

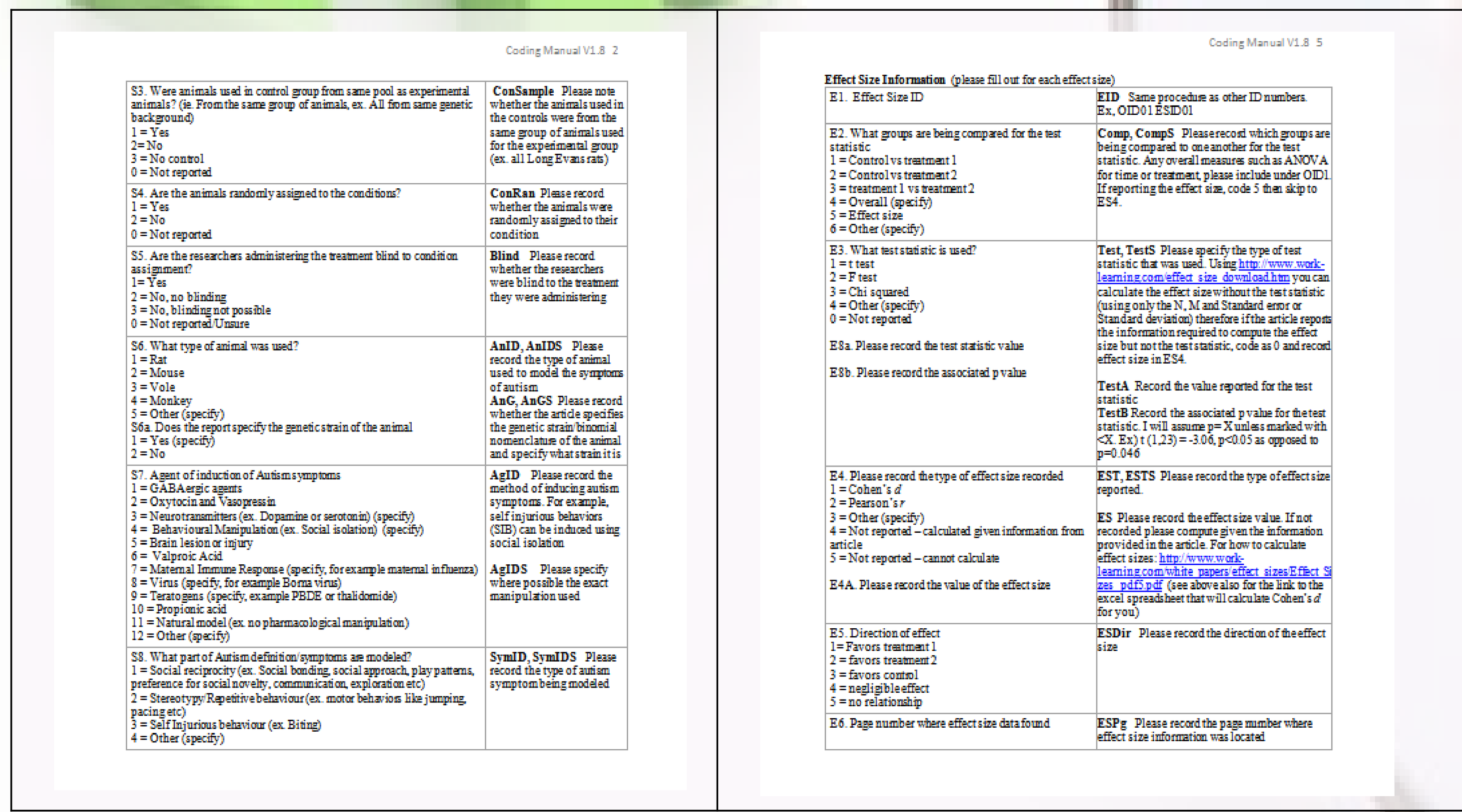
Article selection: Selection based on studies examining effects on behaviour , as well changes in brain areas including but not limited to :the frontal cortex, the hippocampus, and the cerebellum

Coding: Group articles → Effect sizes ← Individual articles

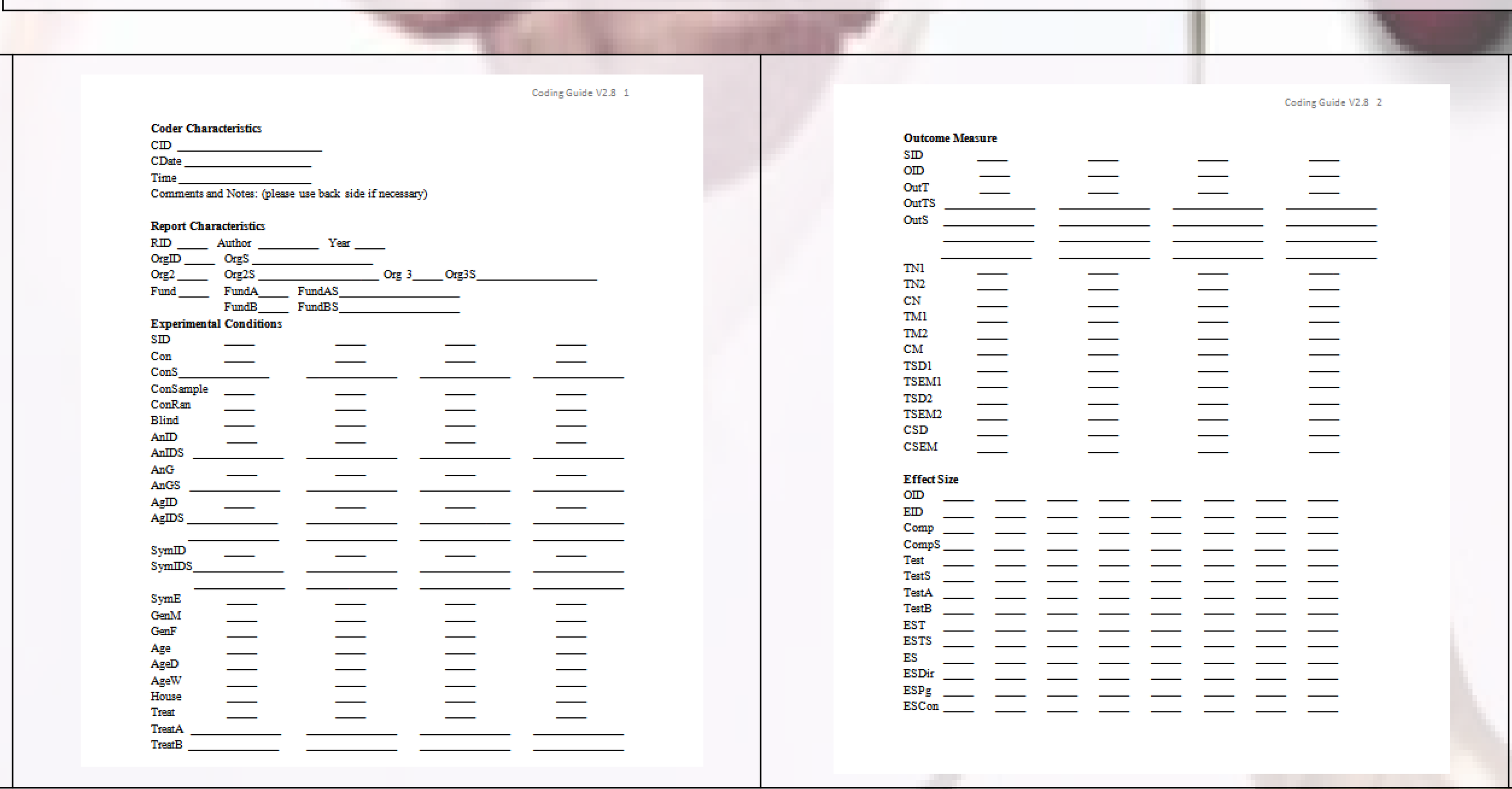
Data entry: Data entry and meta analysis

RESULTS

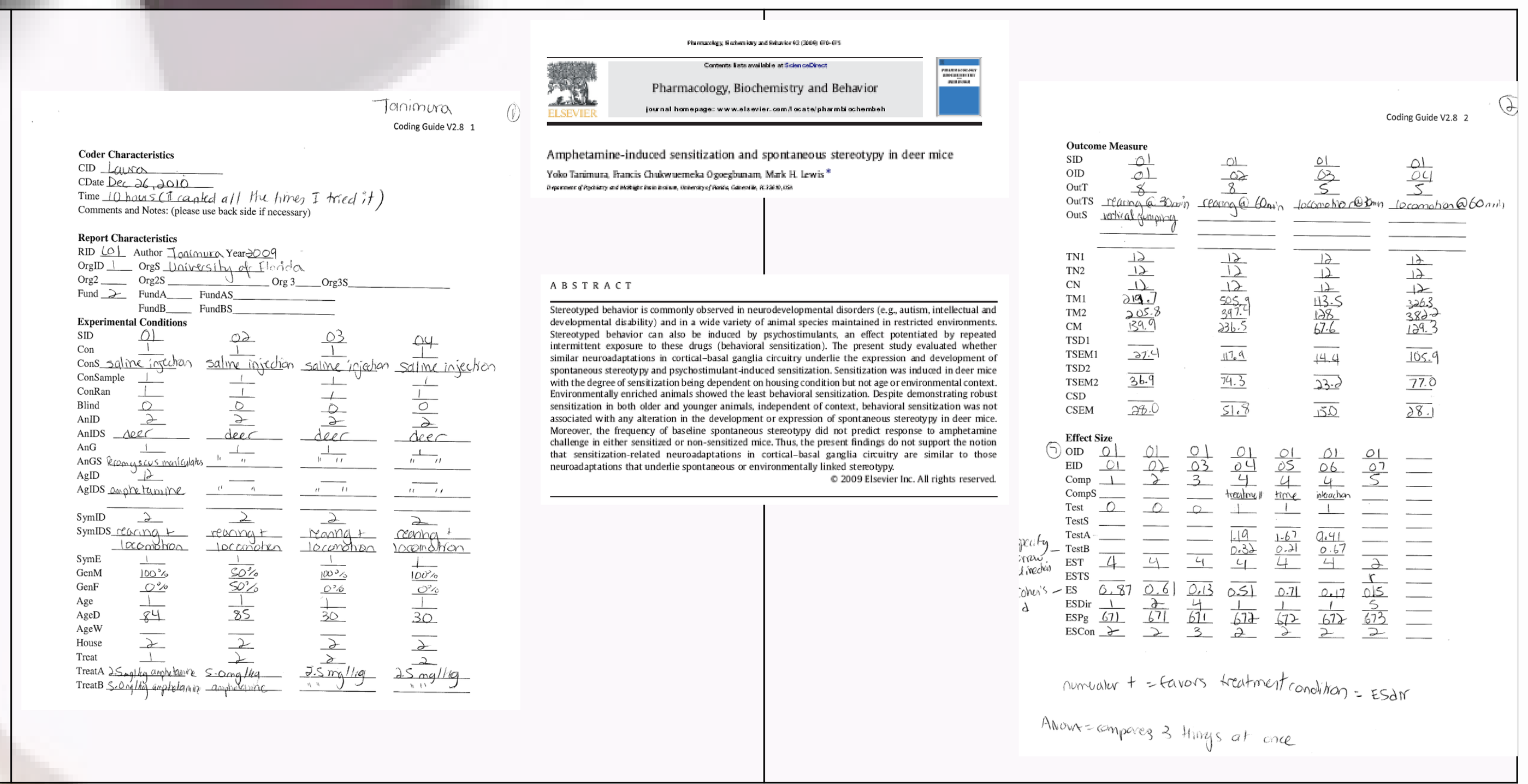
CODING MANUAL



CODING GUIDE



CODED ARTICLE (e.g.)



Summarizing these articles during the coding process gave us the following information:

1. Shultz et al (2008) showed us that contact with valproic acid can produce neuroinflammatory responses in rats, thus impairing their behaviour.
2. Narita et al (2002) demonstrated that exposure to thalidomide and valproic acid increased the levels of hippocampal serotonin and frontal cortex dopamine.
3. The study by Wagner et al (2008) demonstrated that neonatal exposure to valproic acid resulted in damaged cells in the cerebellum that would eventually undergo apoptosis, thus resulting in behavioural deficits.
4. The role of pathogens in autism was also explored by Fatemi (2005) and Meyer (2009). They found that post natal dysfunctions related to infection are dependent on timing and type of viral exposure.

Ultimately, like pieces in a puzzle, these articles all provided insight into how specific characteristics of certain brain areas are affected. By putting these pieces together, one can examine the effects of autism on the brain as a whole. After noting all the variances, a better understanding was achieved regarding why autism is different to treat: all brain areas respond differently to the same stimulus making a generalized treatment difficult to obtain.

DISCUSSION

Limitations of the literature:

1. Work with both sexes: It is undoubtedly of the utmost importance to examine the effects of autism on the male rat brain in relation the inflated frequency of cases within the human male population. On the other hand, virtually all the studies only examined the effects on male rodents, which does not give us any insight into the causes of sexual dimorphism. To view differences between genders, female rat brains should be exposed to the same teratogens as the male brains in order to note the sex differences in neurotransmitters in relevant brain areas.

Limitations of the coding guide:

1. The coders were often confused about how to code specific sections of articles since many of the studies/means of testing didn't seem to fit in any predetermined category, or appeared to fit into multiple categories. Because of the individuality in interpretation, a group of five articles were all coded by all the coders in order to verify reliability.
2. The articles may have presented data in bar graphs or in forms that hindered one's ability to obtain the averages and standard deviations required for the effect size calculations. This could have huge impacts on the reliability and validity of the data entered for the future meta-analysis.

CONCLUSION

Although the lack of studies on female rodents does not provide much insight into the mechanisms of sexual dimorphism in this class of disorders, the pending results of the meta-analysis aim to shed some light on this factor. The coding of articles allowed me to gain some insight into the potential causes for autism spectrum disorders, as well as how specific brain areas are affected. Valproate induced autism (autistic-like symptoms) has proven to be a valuable animal model because it accurately mimics the human condition. The increasing body of knowledge regarding autism is allowing us to better understand how the brain develops and how early life events might impair this development.

A potential area for future research would be to attempt to repair the damaged brain areas. These articles have also explored the possibility of a pathogenic cause for this disorder and its effects on DNA (epigenetic) in various brain areas. Another future direction would be to investigate those environmental toxicants that mimic valproate's teratogenic effects in order to glean some real-life information on the etiology of these disorders.

REFERENCES

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