Neuropsychological Evaluation and Outcomes of Acute Lymphoblastic Leukemia Treated with Chemotherapy in a Transgender Adolescent Male: A Case Study

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INTRODUCTION

Transgender youth face enormous barriers to accessing gender affirming medical care, including the neuropsychological evaluation of complex medical/neurological conditions such as acute lymphoblastic leukemia (ALL) and its treatment. While considerable research exists on the late effects of chemotherapy and other treatments for ALL, evaluating the transgender population brings up additional unique considerations. Normative data for cognitive and psychological measures have not been developed for transgender individuals, creating a dilemma for neuropsychologists. Sex-based differences in certain domains such as fine motor speed, attention, and processing speed (Jäncke, 2018; Miranda, Rivero, & Bueno, 2013; Smith, 1973), along with evidence for brain-based changes following hormone therapy (Karalexi et al., 2020) are additional factors. This creates a dilemma when determining the most appropriate normative group for assessing functioning related to one's medical history while also considering psychosocial factors and providing gender affirming care. The aim of this study is to discuss unique considerations for neuropsychologists when evaluating medically complex transgender individuals.

DEMOGRAPHICS

The patient was diagnosed with Pre B-cell ALL at 2 years of age. Chemotherapy treatment included intrathecal methotrexate and cytarabine; treatment was completed at 4 years of age. The patient did not receive radiation. The patient was assigned female at birth and experienced gender dysphoria beginning in childhood. At the time of the evaluation (age 14) the patient identified as male (he/him). He had a pre-existing history of attention-deficit/hyperactivity disorder, generalized anxiety disorder, and obsessive-compulsive disorder. He was being treated with Strattera and Luvox. He had not yet begun treatment to assist with gender transition (puberty blockers).

NEUROPSYCHOLOGICAL CONSIDERATIONS/FINDINGS

Gender combined norms were used when available. Otherwise, preferred gender norms were used to assess psychosocial/daily functioning with an analysis of confidence intervals across both genders. Norms based on sex-assigned at birth were used within the context of known sex-based differences and low likelihood of brain-based changes at this time. This methodology was determined as best practice following a review of the literature (APA, 2015) and discussion within our neuropsychology department. Estimates of cognitive functioning revealed high average intelligence and average or better skills across direct tests of memory, attention, executive functioning, and academics. Visuo-motor and processing speed skills were variable.

Measure		**Standard Score**	**Scaled Score**
Grooved Pegboard*	Dominant (Right)	96	
	Non-Dominant	98	
Visual Motor Integration*		87	
Visual Perception*		101	
Motor Coordination*		93	
Coding*			7
Symbol Search*			11
Symbol Digits Modalities Test (Oral)**		117	
Behavior Rating Inventory of Executive Functions, 2nd Ed. ***		**Parent T Score**	**Self T Score**
Shift		69	62
Initiate		67	---
Working Memory		82	66
Plan/Organize		72	69
Task-Monitor/Task Completion		59§	68

**Combined norms used; **Female norms used; ***Male norms used*
§All scores are within 90% confidence interval for same-aged females, except for task-monitor (T=65)

Parent and patient rated moderate to significant concerns (T>60) for anxiety, withdrawal, somatization, attention problems, and hyperactivity. Patient denied problems with depression but identified significant symptoms of anxiety compared to same-aged males. (Behavior Assessment Scale for Children, 3rd Ed., Child Depression Inventory, 2nd Ed., Multidimensional Anxiety Scale for Children, 2nd Ed.)

BEHAVIORAL OBSERVATIONS

Patient was cooperative throughout the evaluation. Mild anxiety was observed (shaking leg). There were no observed problems with attention, language, fatigue, thinking speed, or motor.

DISCUSSION

Relatively worse performance on processing speed tasks with high fine motor demands and on drawing tasks may be related to issues with fine motor skills in daily life and neuropathic pain, often an effect of cytarabine (although notably fine motor dexterity was average bilaterally). Issues with attention and executive functioning in daily life may be a late effect of chemotherapy. Intact performance on testing (within the context of parent and patient reported problems) suggests greater difficulty in real world settings perhaps exacerbated by anxiety and other psychosocial factors. Notably, patient and parent reported improved anxiety symptoms since receiving gender affirming psychosocial and medical support.

FUTURE DIRECTIONS

With the rising rate of individuals who identify as transgender (Zucker, 2017) and the known benefit of receiving gender affirming care on one's mental health (Keo-Meir & Fitzgerald, 2017), it is incumbent on us as neuropsychologists to thoughtfully consider norm selection and conduct additional score analysis to ensure the most accurate evaluation. Further research into sex-based neuropsychological differences and the impact of hormone treatment on brain-based functioning is needed.

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