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Fragile X syndrome: Neural network models of sequencing and memory

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Abstract

A comparative framework of memory processes in males with fragile X syndrome (FXS) and typically developing (TYP) mental age-match children is presented. Results indicate a divergence in sequencing skills, such that males with FXS recall sequences similarly to TYP children around five and a half years of age, but the males with FXS recall significantly worse when compared to TYP children around seven and a half years of age. Performance on one working memory measure, an n-back Card Task, is modeled with a neural network. To date, no network models explicate the sequencing and memory processes in those with FXS. Noise was added to various levels (weight matrices) in the FXS model and outputs approximated human FXS performance. Three models were compared: (1) FXS; (2) younger mental age-TYP matches; (3) older reading level-TYP matches. Modeling can help to reify conceptualizations of deficits and to guide in the creation of more valid, science-based remediations. The FXS model suggested that the levels of phonological representation and sequencing in memory were candidates for targeted therapies in males with FXS.

Keywords: Fragile X syndrome; FXS; Modeling; Neural networks; Memory in atypical populations; Phonology; Literacy; Intellectual disabilities

1. Introduction

This article presents a brief, comparative framework of memory in males with fragile X syndrome (FXS) and then describes three implemented computational models of a working memory task focusing two groups of typically developing (TYP) matches.

FXS is the most prevalent form of heritable mental retardation in the world. It affects approximately 1 in 4000 males and 1 in 8000 females (Hagerman, 1999). The mutation consists of an unstable expansion of CGG trinucleotide repeats on the 5′ untranslated region of the FXMR1 gene (Oberle et al., 1991; Verkerk et al., 1991). There is much variability in the symptoms manifested at the cognitive, linguistic, and social levels of functioning. The mutation is X-linked and, on average, females are less affected. Females with FXS present an even wider range of cognitive deficits and psychological dysfunction (Mazzocco & Reiss, 1999). In order to model a group with more severe issues, and less overall variability, the empirical FXS group in this study is composed of males only. The control match groups include both males and females because meaningful gender differences have not been observed in typically developing children on the types of memory measures included in this study (Strand, Deary, & Smith, 2006).

1.1. Profile of cognition in males with FXS

Males with FXS possess relative strengths and weaknesses in the higher levels of cognitive functioning. They have difficulty integrating past experiences with present (Sobesky, Hull, & Hagerman, 1992) and with abstract

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reasoning (Freund & Reiss, 1991). They are resistant to environmental change (Reiss & Freund, 1990), and demonstrate a need for sameness. They often overreact to novelty (Scharfenaker et al., 1996). Males with FXS perform significantly worse on arithmetic measures when compared to the mean performance of children with Down syndrome (DS) and nonspecific retardation (Hodapp et al., 1992). In addition, males with FXS perform significantly worse on hand movement imitation (Hodapp et al., 1992). Regarding some of their relative strengths, those with FXS perform better than individuals with Down syndrome on several processing tasks that are traditionally considered *simultaneous*, e.g., Magic Window (identifying a partially occluded object passing through a window) and gestalt memory closure (identifying partially obscured line drawings) (Hodapp et al., 1992). These results have led researchers to put forth the theory that those with FXS have relatively stronger skills in simultaneous processing vs. sequential processing when compared to other groups with intellectual disabilities (ID).

1.2. Memory research in TYP individuals and individuals with intellectual disabilities

Currently, there is not a clear picture of working memory and its subprocesses in the population with FXS. In the TYP population, children ages 1–12 years demonstrate an age-related linear increase in skill for digit, letter, and word span measures (Dempster, 1981). Cowan (1997) highlights six developmental changes postulated to account for memory increases with age. These changes can occur in (a) knowledge, (b) processing strategies, (c) processing speed, (d) use of attention, (e) passive memory loss over time, and (f) memory storage capacity. All of these are correlated with age and brain growth (in particular myelination). One of our questions was at which point in development would be we begin to see a dissociation in sequential memory between mental age-matched TYP children and males with FXS. As a starting place, the match point of nonverbal skills was chosen; this corresponded in the TYP population to a chronological age of five and a half years.

One reason why precise research on memory in individuals with ID has been hampered is that much of it has neglected effects of etiological specificity. Over the decades, several theories of memory in individuals with ID have risen and fallen in prominence. Ellis (1963) was a proponent of the weak stimulus trace theory (akin to the passive memory loss theory mentioned above). In the late 1960's when strategy theories became influential (e.g., Atkinson & Shiffrin, 1968), researchers investigated rehearsal and processing strategies (Belmont & Butterfield, 1969; Campione & Brown, 1977); the theory was that those with ID did not spontaneously generate strategies. Over the years, all the factors that explain growth in memory in the TYP population, have been specifically postulated as the primary deficit(s) for those with ID, except for lack of attention. This may be because some consider attention an overlying global deficit in most developmental disabilities.

Another reason it is difficult to pinpoint a single memory deficit in groups with ID may be because memory (like cognition) is not a simple unitary process. Memory tests, by their nature, often tap multiple processes. In their thorough meta-analysis, Weiss, Weisz, and Bromfield (1986) report that there is also not a simple, favored outcome when comparing TYP and ID group performances on traditionally Piagetian tasks. Only a minority of the 24 studies analyzed, i.e., 45%, reported a significant difference favoring the TYP mental age-match groups. A finer-grained framework of memory processing strengths and weaknesses is necessary before further analyses should continue. In addition, memory and cognition should not be viewed as static processes.

1.3. Dynamicism

Munir, Cornish, and Wilding (2000) and Cornish et al. (2004) state the case for a developmental approach that does not view cognition as an insulated and modularized construct. Differences at the genetic and brain structure levels from conception onwards effect growth and outcomes dynamically. This point of dynamicism in development and the emergence of relative strengths and weaknesses is advocated by researchers who study both TYP and ID populations (Abbeduto, Evans, & Dolan, 2001; Chapman, 2000; Karmiloff-Smith & Thomas, 2002; Thelen, 1994). Before describing the memory matrix and the measures in this study, it is recommended that the memory subprocesses be viewed as existing on a continuum. For example, many geometric design tasks are categorized as nonverbal, but Howieson and Lezak (1995) warn that these items can be recalled using verbal rehearsal strategies as well. For ease of classification, the simplistic descriptors of *verbal* and *nonverbal* memory are used throughout, but with the caveat that these constructs are conceived of as existing on a continuum and some measures are *more* verbal and some are *more* nonverbal than others.

1.4. Memory: verbal and nonverbal

Baddeley's (1986) theory of working memory has become the standard for parsing memory. Baddeley posits that working memory is comprised of three elements. The first is a central executive (CE) in charge of planning, flexibility, and shuttling information. In addition, it has been proposed that the CE is in charge of more specific skills such as switching, updating and inhibition (Miyake et al., 2000). The CE system contains two sub-systems, the articulatory or phonological loop and the visuo-spatial sketchpad. Visuo-spatial tasks in this study often map to the simultaneous spatial processing (e.g., replacing toys correctly on a table). Phonological tasks map to the phonological loop which is deemed to be part of a more sequential system – especially when multiple words must be concatenated and recalled.

Baddeley's model has been, rightfully, extremely influential but it can no longer concisely accommodate many recent empirical findings. There is now an alternative to