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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 eth 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; and 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 suggests that the levels of phonological representation and sequencing in memory are candidates for targeted therapies in males with FXS.

### Keywords

Fragile X syndrome; FXS; modeling; neural networks; memory in atypical populations; phonology; literacy; intellectual disabilities

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 4,000 males and 1 in 8,000 females (Hagerman, 1999). The mutation consists of an unstable expansion of CGG trinucelotide 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

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children on the types of memory measures included in this study (Strand, Deary, & Smith, 2006).

## 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 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 versus sequential processing when compared to other groups with intellectual disabilities (ID).

## 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 through 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 there has been a lack 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 (Bellmont & 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 Broomfield (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.

## 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.

## 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 the concept of working memory as modularized slave systems and mention should be made of Postle’s (2006) theory that working memory is an emergent property of mind and brain. Postle’s hypothesis is that working memory’s functions are not supported by multiple specialized systems -- that include the prefrontal cortex (PFC) acting as a temporary storage area -- but that working memory phenomena arise through the coordinated recruitment, via attention, of brain systems that evolved over the millennia to do various tasks corresponding to sensory-, representation-, and action-related functions. This theory dispenses with the redundancy inherent in Baddeley’s standard theory, i.e., that information is somehow shuttled to the PFC to be looped and maintained. The theory states that activation of information to be remembered in the short term is located in the same brain regions that coded for the representation in a non-working memory situation, e.g., “perception, semantic memory, oculo-and skeletomotor control, and speech comprehension and production” (Postle, 2006, p. 35). Besides being parsimonious and supported by recent fMRI studies, this theory more elegantly meshes with embodied accounts of cognition and language that implicate modality-specific systems in the representation and use of conceptual knowledge (Barsalou, Simmons, Barbey & Wilson , 2003; Glenberg & Kaschack 2002). Throughout the paper, interpretations of how both memory camps (standard vs. emergent) might interpret outcomes is made.

Keeping both hypotheses in mind, we will ask how the memory outcomes differ between the populations and propose recommendations for remediations. The working theory was that the FXS group should perform equal to, or somewhat better than, the matched-TYP groups on the more verbal and simultaneous tasks - like vocabulary or the recall of one item on an n-back task. This was because the FXS group is older (and perhaps had more world knowledge) and because lexical level knowledge will not have to be sequenced on a one item task. Abbeduto et al. (2003) found that the FXS group significantly out-performed a Down Syndrome (DS) match group on the TACL (Test for Auditory Comprehension of Language-Revised; Carrow-Woolfolk, 1985) - which tests receptive language. Thus, there is some evidence that males with FXS possess relative verbal strengths compared to other ID groups. But, what about recall after a delay?

## Recall: Immediate and delayed

Another important distinction in memory is that between working (short-term) and long-term memory. The two memory systems complement one another as learning systems. That is, new information passes through the prefrontal areas and the hippocampus (HC)[1] - among other structures. The HC is designed to rapidly encode, assess, and redirect novel input from the information stream. Neuroscientists agree that the HC plays an important role in learning and memory, but consensus has yet to be reached as to the exact role (Gluck & Myers, 2001). One theory is that new information is “slowly interleaved” with long term memories that are stored more neocortically (McClelland & Goddard, 1996;McClelland, McNaughton, & O’Reilly, 1995). Learning is the result of this complementary meshing of old and new information.

Another distinction in long term memory is between declarative and procedural. The declarative system (Schacter & Tulving, 1994; Ullman, 2004) has been implicated in the learning, representation, and conscious manipulation of events (often called episodic knowledge) and facts (often called semantic knowledge). These events and facts can be consciously recalled. The procedural system (Squire & Knowlton, 2000; Ullman, 2004) is implicated in the control of established sensori-motor and cognitive skills (implicit skills) and “procedures”, e.g., riding a bicycle. This system may be especially important in the learning of real time sequences (Ullman, 2004), and it is here that the basal ganglia plays a large role. Declarative and procedural distinctions are favored by cognitive scientists and neuroscientists, while in the Intellectual Disabilities field more descriptive emphasis is placed on the explicit requirements of the tests used. For example, although the hand movements task involves the recreation of motor sequences and might be considered *procedural*, it is reproduced immediately after viewing the experimenter and could also be stored as a “conscious” event rather than as an implicit string (that is, *declarative*). Thus, for the purposes of this study it seems clearer and more precise to refer to a measure like the hand task as “nonverbal and sequential”. In this study, three tasks were given again after a delay - they might be considered more *declarative*. However, in keeping with the descriptive matrix favored by the ID field, these tasks will be described as verbal or nonverbal and dependent on either simultaneous or sequential processing.

## Processing: Simultaneous and sequential

This distinction came to prominence based primarily on findings by Hodapp et al. (1992) and Dykens, Hodapp, and Leckman (1987). Hodapp et al. (1992) assessed three groups: males with FXS, individuals with DS, and individuals with ID of nonspecific etiology. Sequential processing was measured using three subtests from the K-ABC (Kaufman & Kaufman, 1983): hand movements, number recall, and word order. The FXS group performed

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[1] Due to space constraints, the many other brain structures involved in learning will not be described.

significantly worse than the DS group on hand movements. Using a within-group analysis on the K-ABC results, Dykens, Hodapp, and Leckman (1987) reported that males with FXS performed significantly better in the simultaneous domain (again, magic window and gestalt memory subtests) compared to the sequential.

In contrast, Munir, Cornish, and Wilding (2000) do not report a comparative strength of simultaneous processing on the classic spatial memory task from the K-ABC. Their FXS group performed significantly worse than the verbal mental age-match group with DS, the TYP verbal mental age-match group, and the TYP chronological age-match group. It should be noted, however, that the spatial memory task from the K-ABC may not represent a pristine spatial task, i.e., simultaneous, because the final stage of assessment involves serialization of objects for recall. The participant must sequentially point to each empty grid cell where a previously viewed object may have been located.

In addition, it appears that many sequential tasks are phonologically mediated using subvocal rehearsal strategies. In our lab, we witnessed many times the spontaneous use of vocalization to recall serial *spatial* tasks. Thus, one of the hypotheses in this current study is that males with FXS will perform poorly across the board on sequential tasks, regardless of whether these tasks are deemed more verbal or nonverbal. This is because phonological processing is not a strength in males with FXS (Johnson-Glenberg, 2003; Buckley & Johnson-Glenberg, 2008), so verbalizing would not be used as a spontaneous strategy for recall.

## Sub-Processing: Phonological

Whether an individual uses a modularized “phonological loop” or maintains rehearsal of the phonemes in the region of initial activation as per the emergent memory hypothesis, it can be agreed that well-defined and crisp phonemic representations are important. Beyond the unnatural lab world of n-back tests, lies the very real and rich world of reading. Phonological processing has been heavily researched the past couple of decades because it is a key component in decoding (sounding out words) and processing connected text. For all types of individuals, even after partialling out IQ, later reading ability is predicted by phonological processing (Stanovich, Cunningham & Feeman, 1984; Siegel, 1993). Conners et al. (2001) gave several language and phonological measures to a mixed etiology group of individuals with ID. The participants were either relatively stronger or weaker decoders with IQ’s that ranged from 40 to 70. When age was covaried out Conners et al. found that the most reliable difference between the two groups was the ability to refresh phonological codes in working memory. The refresh score was a composite measure comprised of the mean Z score of 1) the difference between repeating three or four syllable words and 2) the Z score for individual articulation speed (which also relies on crisp representations).

The ability to read has enormous implications on quality of life. There is large variability in the reading skills of individuals with ID. One of the goals of this article is to begin charting some of the strengths and weaknesses in males with FXS as they relate to several reading subprocesses. The ability to sequence phonemes is necessary for the sounding out of novel words. In order to further assess the simultaneous and sequential processing domains in males with FXS, two classic decoding tasks were administered: 1) real word reading - theorized to map primarily to simultaneous processing because the well-established lexical route would analyze a known word as one chunk (Ehri, 1992), and 2) a nonword reading task - theorized to map primarily to sequential processing because the novel phoneme sequences would require both phonological processing and assembly (sequencing) skills. In order to make more precise sequencing comparisons, a third group, a TYP reading-match group, was created later in the study and will be described before the modeling section.

Table 1 demonstrates the proposed 2 X 2 X 2 memory framework. The group displaying the predicted relative strength is listed in each cell. The final cell is empty because there was not an appropriate nonverbal, delayed sequential test at the time of the study.

In sum, several standardized and experimenter-designed measures were administered to typically developing groups and to a group of males with FXS in order to assess the strengths and weaknesses in various memory and processing domains. Of particular interest is the n-back Card Task which taps into sequencing and will be modeled in the second section. We had predicted that the FXS group would perform significantly worse on sequencing tasks because they have traditionally shown a weakness in sequential working memory. Modelling should help to pinpoint where this weakness might reside - at the representational level or at the looping/refreshing level. The ability to sequence is important for higher level cognitive functioning, but is crucial for reading. The article ends with recommendations for types of targeted cognitive and reading remediations.

## Method

### Participants

Three groups of participants were studied. The first group consisted of 15 males with FXS, age range 11;5 to 38;1 (m = 20;6); the second consisted of 22 TYP mental age matches, age range 3;11 to 8;3 (m = 5;5); and the third group was formed later in the study and consisted of TYP Word Identification-match children, age range 5;4 to 8;3 (m=7;6). For this final group, seven of the mental age-TYP group were retained and six new participants were tested. The new Word ID match group is on average two years older than the first mental age TYP match group.

Participants with FXS were recruited through postings on the Internet at national fragile X foundations, through advertisements in newsletters of regional organizations that serve individuals with ID, and via mailings to local genetics clinics and doctors who specialize in developmental and intellectual disabilities. TYP children were recruited through a University-based birth registry. Parents of TYP children indicated their children had no history of special education or hearing loss at the time of the study. English was the first language of all the participants. FXS status was confirmed via doctor and geneticist reports provided by the parents. Four of the oldest participants (all over 28 years) were diagnosed through karyotype screening.

The FXS group was 100% male and contained one Hispanic male and one African American male. The TYP mental age-match group was 55% male and contained one boy of Hispanic origin. The TYP word ID - match group was 54% male.

### Materials

Eleven tests were administered to three groups of participants. One test, the Phonological Awareness Test was administered to only a subset of the FXS group.

**Grouping Variables - Mental Age—**Mental age was assessed with two separate measures. The shorter Columbia Mental Maturity Scale (CMMS) was administered to nine TYP and three FXS participants when it became obvious that the males with FXS were displaying a position bias effect.[2] Because this sort of test does not seem valid, nor reliable, for the FXS population, the decision was made to use the Stanford-Binet (4th ed.) (Thorndike, Hagen, & Sattler,

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[2] The CMMS is based on the odd-one-out concept. Participants must pick which image does not belong on a long cardboard card (e.g., cup, magnifying glass, knife, glass, fork). When the experimenter noted the position bias (after a streak of five), it was brought to the participant’s attention, “Remember, it is not always the third item.” This did not appear to break the participant’s perseveration or mental set.

1986) subtests of Bead Memory and Pattern Analysis. These subtests have been used extensively with individuals with developmental disabilities (Abbeduto, et al. 2003;Miles & Chapman, 2002) and they scale properly for delayed populations. The CMMS maturity index scores map to the Stanford-Binet's age-equivalents scores. The correlation of the CMMS with the first version of the Stanford-Binet is .67 for TYP children, and .61 for children with ID (French & Worcester, 1956).

**Bead Memory—**Stanford -Binet 4th ed. (Thorndike et al., 1986). Depending on level attained, participants either view beads in the experimenter's hand, or view a picture and then name or recreate the bead sequence on a stick.

**Pattern Analysis—**Stanford -Binet 4th ed. (Thorndike et al., 1986). Depending on level attained, participants either place geometric forms onto a board, or recreate the design the experimenter has constructed.

**Reading Measure—***Word Identification* - (Word-ID) Woodcock Reading Mastery Tests-Revised (Woodcock, 1998). Participants read real words from an easel booklet until six consecutive errors are reached on a page.

**Reading Measure—***Word Attack* - Woodcock Reading Mastery Tests-Revised (Woodcock, 1998). Participants read nonwords from an easel booklet until six consecutive errors are reached on a page.

Table 2 lists the results of the grouping variables and t-tests comparing the TYP groups to the FXS group.

**Testing Variables - Attention - Continuous Performance Task (CPT)—**This test is an experimenter-designed computerized task based primarily on Crosby's (1972) CPT task. Part I measured simple attention ("Hit the key when you see the red square."); Part II measured impulsivity ("Hit the key only if the red square was preceded by a blue triangle"). The groups appeared to be matched on attention, e.g., Part I resulted in equal D primes for both the FXS and MA Match TYP groups: FXS = 2.63 (1.45); MA TYP Match = 2.62 (1.07), $t < 1.0$. Because the groups did not differ on this more upstream processing variable, it will not be described further.

### Memory Measures - More Simultaneous (Spatial)

**Toy Recall—**In an effort to assess simultaneous memory in an engaging manner that would lend itself to a delayed component, a classic spatial task used by Smith and Milner (1981) was slightly altered. Participants were asked to immediately verbally recall, and then recreate physically the placement of 16 toys on a table top after a 2.5 hour delay.

**Gestalt Closure—**K-ABC (Kaufman Assessment Battery for Children- Kaufman & Kaufman, 1983). This subtest measured the participants' ability to "fill in the gaps" in a partially completed inkblot drawing. Participants named (labeled) the image. It is our contention that for the younger children, the test is also very dependent on vocabulary skills. The intercorrelation between Gestalt and the K-ABC Expressive Vocabulary is .47 (Kaufman & Kaufman, 1983) for preschool children. This is one of the highest intercorrelations seen between all the K-ABC subtests. We felt forced to make a decision as to which process it primarily tapped into and decided that since the scoring criteria had been flexible for labeling (i.e., if a child said "something to boil water in" instead of "tea kettle" he/she was scored correct), the test was prpbably a better indicator of perceptual recognition. Thus, it is listed under immediate, nonverbal simultaneous processing.

### Memory Measures - More Sequential

**Card Task—**This task is an experimenter-designed measure and the one that will be modeled so it is described in some detail. It is a developmentally appropriate running n-back memory span test. The experimenter and the participant face a laptop. On the screen are three decks of cards, the bottom two decks are face down and belong to the experimenter and the player. The upper deck placed in the middle of the screen represents the discard pile. See Figure 1. The experimenter hits the space bar to control presentation of a card (i.e., to "flip up" a card) to the discard pile, and the participant hits any button on the mouse to flip up a card. These actions alternate. At quasi-random intervals, the experimenter hits a key that prompts for recall. That is, a graphic of a hand appears and covers the discard pile. Before prompting a recall the experimenter must wait until a set minimum number of intervening cards have appeared *and* must also monitor that the participant's eyes to assure they have been on the screen throughout the sequence. The system does not allow the cards to be displayed at a rate faster than one card every two seconds. (Figure 1 also shows an example of a dog "distractor". Distractors and attention issues are discussed in Johnson-Glenberg, 2007a).

The participant is asked to recall the last card(s) viewed. The number of cards to be recalled varies by set. There are four sets of one, two, three, or, (if attained) four cards recalled in a sequence. Single cards that are recalled after a sequence of intervening cards are called "onesies", two cards are called "twosies", etc. In each set there are four onesies, six twosies, three threesies-- and if one threesie is recalled correctly, then three more threesies and two foursies are presented. Because none of the individuals with FXS got any of the foursies correct, those data will not be reported.

Before scoring begins participants practice a onesie recall on the computer, then they practice a twosie recall with a real deck of cards. The real deck is used to teach the concept of recalling the card "on top" - the one closest to the hand - as the first card. (Piloting revealed this to be the preferred order of recall.) Participants practice with the real deck until they are correct. Participants then practice a twosie and a threesie on the computer.

The card task is also divided into two blocks. The first block is color only, consisting of red, green, yellow, and blue cards; the second block is color and number (col&num), consisting of the same four colors with the numerals 1, 2, 3, or 4 embedded in the middle of the colored card. Thus, there are 16 different cards in the second block and two pieces of information, or components, that must be recalled (e.g., "red three") for each card. Block 2 is more difficult than block 1.

**Verbal Auditory Learning (VAL)—**Woodcock-Johnson III, Tests of Cognitive Abilities (Woodcock, McGrew & Mather, 2001). Participants are first taught rebus symbols for words and then they *read* sentences written with the symbols. This test includes an immediate and delayed portion, approximately 1.5 hours later.

**Hand Movements—**K-ABC (Kaufman Assessment Battery for Children- Kaufman & Kaufman, 1983). This test measures skill in imitating an experimenter's hand movements on a table top. The movements consist of a series of taps from a fist, flat palm, or side of the hand. This task is included because it has strong non-verbal components, although even the interpretive manual (Kaufman & Kaufman, 1983) admits that using mediating strategies, e.g., verbally labeling, would aid in performance. The purity of the measure may be further clouded by motor planning and execution issues.

**Testing Protocol—**Participants were tested individually in a sound-attenuated room at a university research center. Software was administered via a SONY VIAO PCG-FX240 laptop, the card task software was written in E-Prime Beta and 1.0 versions. Measures were given in an invariant order. First, the toy task was administered, then Continuous Performance Attention task, then the mental age and memory tests, then the card task, and finally the two surprise delay tasks.

## Results

Table 3 lists the results from the memory measures comparing the FXS group with the MA matched group. The higher-performing (favored) group is bolded.

### Memory - More Simultaneous/Spatial

**Toy Recall—**The 2.16 toy recall difference between the groups was a statistical trend (i.e., the two-tailed *p* value was greater than .054 and less than .104) that favored the FXS group. (There was no significant difference in the delayed toy recall.)

**Gestalt Closure—**The FXS group performed significantly better on the Gestalt closure task.

### Memory - More sequential

**Card Task—**Results of the t-tests on the Card Task indicate that the two groups did not differ on percent correct in each set of the onesies, twosies, or threesies. Results for the onesies are listed in Table 3 under Verbal Immediate Spatial (rather than sequential, because participants were only recalling *one* item, the very last item seen). The results for the twosies and threesies are listed under Verbal Immediate Sequential. Again, the FXS and MA-matched groups did not differ significantly in recalling cards. This had *not* been our prediction - we had predicted that MA-matched children with a mean nonverbal mental age of approximately five and a half would be better at sequencing and recalling than the FXS group.

**Verbal Auditory Learning (VAL) - Verbal Sequential—**In the delayed version of the VAL (given approximately 1.5 hours later) the TYP group further extended their lead in symbol reading skills, making only 28.67 errors compared the FXS group's 49.43 errors.

**Hand Movements- Nonverbal - sequential—**Results significantly favored the MA-match TYP group.

**Toy Placement- Nonverbal - delayed - spatial—**When asked to replace the toys after an approximate two hour delay, the MA-match TYP group deviated 14.26 centimeters from the point of original placement (the average for all 16 toys). The FXS group deviated 18.07 centimeters. The group differences were not statistically significant.

Table 4 demonstrates how these results map to the predictions made in the Table 1 matrix.

When comparing the FXS group performance to TYP nonverbal mental age-matches, those with FXS showed a trend towards better performance on one of the simultaneous tasks in the immediate verbal realm, and they were significantly better in the immediate nonverbal realm. However, the verbal immediate difference is clouded by the fact that the groups performed equivalently on the Card Task. This was not what we had predicted in Table 1. We had predicted that the males with FXS would perform better across the board in the simultaneous realm and then significantly worse in the sequencing realm for all immediate tasks. These results complicated the plan to model the Card Task - it's not so intriguing to model sameness. It is generally agreed that males with FXS perform poorer on sequential tasks, many match group studies have demonstrated this. Thus, the question became - at which point along the developmental trajectory would males with FXS and TYP children diverge in sequential processing?

If a difference was not evident using a nonverbal mental age-match group, then perhaps the FXS group should be matched using a variable associated with a later developmental age. In a post hoc review of the profile of males with FXS, the construct of reading stood out as a relative strength. Table 2 shows that the FXS sample was reading real words almost two years ahead of the MA-matched group. Therefore, a word reading or word identification (Word-ID) TYP match group was created, and it ended up being, on average, two years older than the MA-matched group.

**Card Task Results with Word ID matches—**When the Word-ID matches were compared with the males with FXS, significant differences were seen on Card Task performance. This warranted further analysis and so the Card Task sets were broken down into their components. For example, in the color and number block there were six trials for the twosie set. In these trials a total of 24 components needed to be recalled. Table 5 lists performance and results on these components.

In the color only block the TYP Word ID group consistently and significantly outperformed the FXS group. In the color and number (col&num) block the component analyses revealed trends or significant differences between the groups. From twosies onwards the col&num trials were difficult for both populations; only four of the FXS participants made it to the threesie col&num set. These results support the contention that males with FXS may be able to perform sequential memory tasks similar to nonverbal mental age-match TYP children around five years of age, but when compared to reading-match TYP children around seven years of age, the males with FXS performed significantly worse.

## Memory Discussion

### Simultaneous/spatial processing

The results indicate that males with FXS demonstrate some relative strengths compared to TYP MA-match children. In the simultaneous verbal processing realm, males with FXS demonstrate impressive effect sizes ranging from .76 to 1.52 when performance is compared to the TYP MA-match group on immediate-toy recall and gestalt memory. On the other hand, the groups performed equivalently on the onesie Card Task - so we can't say that this is an unequivocal strength. Table 4 supplies a succinct summary of the memory tasks and favored groups. The primary task favoring the FXS group is simultaneous, *non*verbal, and immediate. Indeed, gestalt memory has a history of favoring FXS groups (Hodapp, et al. 1992). The task taps two cognitive components: perceptual recognition and object naming at the lexical level, although the pictured objects were probably common enough for the young TYP match group's lexicon. It is therefore probable that the better performance was due to better nonverbal, perceptual processing skills in the FXS group. Future studies should include vocabulary measures so that vocabulary/world knowledge effects can be ruled out definitively.

### Sequential processing

It is apparent that all sequential and delayed tasks - especially in the verbal realm- favored the TYP groups. From this we can begin to extract which processes may be compromised in those with FXS. One candidate is sequencing. What makes sequencing so difficult?

Sequencing is complex - it involves: 1) encoding the information string, 2) holding or rehearsing the string (using a phonological/lexical loop or maintenance activations), 3) concatenating incoming components, 4) for recall - retrieving the components, 5) motor planning for reproduction (e.g., hand movements, articulatory muscles, etc.), and finally 6) actual reproduction of the string. We hypothesize that there were no serious problems at the first and final levels of encoding and reproduction as the males with FXS performed almost equivalently to the TYP children in the onesies condition (col&num) on the Card Task. The sequencing problems may reside in stages 2, 3, 4 and/or 5. Because the groups performed equivalently on the CPT (attention task), it may be assumed that differences on the memory measures and the Card Task were not artifacts of more upstream cognitive functioning related to initial attention of the test elements.

Somewhere along the TYP developmental trajectory between the mean age of 5.5 and 7.5, the cognitive processes responsible for sequencing and recalling information begin to surpass the average performance levels of our sample of males with FXS. To better understand this divergence, it may be helpful to create a model of a sequencing task. Modeling can aid in conceptualizing the components involved in sequencing and working memory. Modeling also allows one to test hypotheses in disabled populations by altering the functioning of the system (in this study - adding noise to the weights) in an attempt to pinpoint where processing problems might be located and how such problems differentially affect outcomes.

**Neural Networks—**Neural networks are powerful computational systems that “mimic” the flow of information through neurons. As a core competency, neural networks are able to learn pattern regularities, even in very complex environments. One of the persistent issues that those with ID face is learning complex, higher level cognitive tasks. Researchers have begun to use modeling to explore developmental disorders, some examples include autism, (Cohen, 1994; Gustafsson, 1997), Williams syndrome (Karmiloff-Smith & Thomas, 2002; Thomas & Karmiloff-Smith, 2003), and developmental dyslexia (Harm & Seidenberg, 1998; Plaut, McClelland, Seidenberg & Patterson, 1996; Seidenberg & McClelland, 1989). To date, no models have been created to explicate the memory and sequencing processes in individuals with FXS. Three models of the Card Task are presented below, these represent functioning in a group of males with FXS, a TYP mental age-match group, and a TYP Word ID-match group.

## The Architecture

The final model presented in Figure 2 went through multiple instantiations. The original architecture for the model was based on Burgess and Hitch (1999), then Jensen and Lisman (1998), and penultimately Elman’s (1990) simple recurrent networks designed to predict the next phoneme in a string of phonemes using context nodes (similar to time bins). This final model is based on O’Reilly and Soto’s (2002) phonological loop model.

The four sets of inputs are on the bottom left. Phonemes and words are used to encode, name, and maintain the Card Task stimuli in verbal working memory and are activated simultaneously to represent the ‘concept’ of the card. Both the phonemic and lexical levels were included because we wanted to analyze the effects of noise on each separate level. The guiding hypothesis was that having weak phonology would be more detrimental to sequential memory because it would compromise the strength of the lexical representations in a very fundamental manner - the system would be unable to recover if the building blocks of the words themselves were compromised. This is a developmental model starting at an age when TYP children are learning to read. Thus, it is conceivable that the phonemic levels might be activated even as a word is unitized. Harm and Seidenberg (1999) have modelled effects of literacy that occur back onto the phonological representations themselves. Thus, it can be assumed that the lexical and phonemic levels are bi-directionally influential on one another for many years. Although this current model is not designed to utilize these types of fine-grained iterative effects, the activations of both the word and phonemic levels are processed by the same pool of hidden units. In addition, imaging research between TYP children and those with dyslexia reveals that different regions of the brain are used for processing real words and nonwords and these regions vary significantly depending on group (Shaywitz & Shaywitz, 2005).

The 17 phoneme inputs are the ones necessary to express the words *red, green, yellow, blue, one, two, three,* and *four*. Time has a localist representation. The four time input units represent order in which the cards are encoded. The four time bins located on the upper right of the graphic correspond respectively to the four time inputs. Hand is binary -- either on or off. If *off* the model passes the input activation from the hidden units to the appropriate time bin and then is ready for new input - the card task continues. If the hand is *on*, the model goes into recall mode. For example, if the to-be-recalled sequence is a twosie, the number 2 ($t_2$) time bin is activated and passes its information to the hidden units, which then process activation out to the outputs. The output for $t_2$ is recorded. Next the number 1 time bin is activated and passes its information to the hidden units (then to outputs). That $t_1$ output is also recorded and the sequence is then compared to the correct input and errors are tallied. This backward sequential order simulates a participant recalling cards in a backward order of presentation. [3] Figure 3 provides a sequential schema of the steps in the model.

The hidden layer is a 15 X 10 matrix dedicated to internal processing and is not directly connected to the environment as input or output. It can be conceptualized as the Central Executive in a standard working memory model or the region of initial activation in a more emergent model. The time bins (called *stripes* in a context layer by O'Rielly & Soto, 2002; O'Reilly Busby, & Soto, 2003) represent the gating function posited between the basal ganglia and prefrontal cortex (O'Reilly, Busby, & Soto, 2003; O'Reilly & Frank, 2005) or the attention-based reactivation factor in the initial activation areas in the more emergent vernacular. Each bin represents a time step. As each card is presented to the system its pattern from the hidden units is shuttled to the appropriate time bin (the second card in a potential twosie would reside in time bin two). Participants know ahead of time which set they are in - so, in a twosie recall they would only be giving attention to each two card sequence. In actuality, the model could not learn when multiple intervening cards were added to the training and so only the to-be-recalled cards were used for training.

Output is localist at the spoken word level. The node with the highest level of activation wins. In Figure 2 the model's input is *yellow*; however, the output node with the highest level of activation is *blue*, and so this would be considered an error.

## Model parameters

The model was implemented using standard simple Leabra algorithm parameters. (See O'Reilly & Munakata (2000) for details.) Software for the PDP ++ Neural Network Simulator was downloaded from http://psych.colorado.edu/~oreilly/. This project's retrieval date was Fall 2004. The learning rate was set and maintained at .01. The Leabra default has self-projection connections on the time bins that loop back onto themselves set at 1.0. This means that at each time step the time bins refresh to the same magnitude. In order to add passive memory decay to the system (Baddeley, 1986), the weights on the self-projections were attenuated to .80 for this model. Multiple models with differing parameters for decay were not analyzed, instead memory looping problems were addressed by adding noise to the weights heading from the time bins back to the hidden units.

To sum up the model, a card is presented in the sequence and the appropriate inputs are received by the hidden units. Figure 2 represents a participant who has just seen a yellow card at time 1. The hand is in the off mode so the system expects another card to be encoded (i.e., do not recall yet). The activation travels from the hidden units matrix - where the weights and

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[3] Participants defaulted to this order of recall- and we also reminded/trained them to that. We should also note that other network variations were created, in one we clamped visual-spatial representational inputs acting as pre-inputs, but these levels have been removed for ease of interpretation. It was assumed that all participants (hence models) had well-defined visual inputs and motoric/expressive outputs because all were screened on a naming task and with an informal intelligibility task.

activation levels are multiplied, summed, and squashed - to the appropriate time bins. The second card's representation would occupy time bin 2. The participant knows this is a twosie ahead of time, thus the model is also constrained to not pass activations into bins 1, 3 and 4, but to send activation from the hidden units straight to bin 2. When the hand input is in *on* mode (activation = 1.0) it is time to "recall" and no other activation flows from the other inputs. Only the pattern from time bin 2 is queried and that information flows back to the hidden units and on to the outputs. This would be recorded. Next, the pattern from time bin 1 would be queried and flow back to the hidden units, on to the outputs and be recorded. Those two sequential outputs would then be compared to inputs for errors and then to the average of human group comparison.

Connections can be conceptualized as bundles of neurons. Extending this metaphor, certain claims about localization can be made. In addition, connection levels represent various cognitive and memory constructs. To simulate dysfunctional processing, noise was added across the weight connection matrices (i.e., not at the input level). These noise and functioning levels map to *a-d* in Figure 3:

Levels-

1. Phoneme to hidden - This level of weights passes phonemic activation to the hidden units. The phonological representations are assumed to be located in the superior temporal sulcus (STS, Scott, Blank, Rosen & Wise, 2000) and the "dorsal circuit" associated with early reading (this temporo-parietal circuit includes the angular gyrus, supramarginal gyrus, and the posterior aspect of superior temporal gyrus - STG: Pugh, et al. 2001). The phonemic level would then project to many other brain areas, including working memory areas- be those in the PFC for representation and looping or at initial site of activation per the emergent philosophy. The hidden units are conceptualized as working memory processors and most of the activity related to the Card Task might occur primarily in the lateral PFC (per fMRI research on humans with n-back span tasks - D'Esposito, Postle, & Rypma, 2000). In our model, it is assumed that stronger phonological activation means that a crisper more distinct level of phonemic representation (Elbro, Borstrom, & Petersen, 1998) is being transferred to working memory. Distinct implies that there are low levels of noise associated with a given signal.
2. Word to hidden - These connections are from the lexical/word level representations (located primarily in the left occipital/temporal region - including lateral extrastriate areas, Pugh et al. 2001) to the hidden units. Again, the hidden units are conceived of as the working memory processors - maybe primarily lateral prefrontal cortex. It is assumed that stronger activation means a crisper level of representation with less noise.
3. Hidden to time bins - These connections project from hidden units (working memory) to the time bins (sequencing arena). In the standard memory model these connections would represent the first stage in the phonological loop process. This direction of flow represents a cascade from prefrontal to more medial brain areas. The hypothesis is that the basal ganglia (O'Reilly & Frank, 2005) is involved in sequencing/gating. It is assumed that stronger activation means a faster, better defined signal and highly synchronized processing.
4. Time bins to hidden - These connections represent the flow back from scenario three. This direction is the opposite cascade, and now information is returning from the more medial location to the prefrontal areas where it is readied for evaluation, motor planning, and articulation. These connections simulate a component of the retrieval system and are dependent on a well-defined and highly synchronized timing signal.

Because retrieval decays over time, cycle-contingent degradation (.80 refresh) has been added to the signal in the time bins at each new cycle. Thus, the signal returning to the hidden units will be more decayed than when it left.

### Methodology

Three models were analyzed. Those models awere: 1) Younger TYP MA-Matches, 2) Older TYP Word ID-Matches, and 3) males with FXS. For simplicity and the purposes of the upcoming analyses, the TYP match groups are referred to as 'younger' and 'older' TYP. Recall that the younger TYP and FXS groups performed equivalently on the Card Task. However, the older TYP group performed significantly better on the subcomponents analysis of the Card Task. To simulate developmental growth, the training on the TYP model was stopped when the error rate resembled the young TYP children's errors (*M* age = 5;5). Training then resumed on the same model until it resembled the performance of the older TYP children (*M* age = 7;6).

### Training and generalization sets

In order to train and test the models, the three datasets were randomly halved. One set was used for training the system, and the other set was used for testing the fit. It is important to not overfit the first trained model because the model will then be a poor predictor when given a new (test) dataset. Data from seven randomly chosen participants in each group were used for training. The trained models fit the new data to an acceptable Mse of 20.

The average number of Card Task errors per components was tallied for each group. For the training sets the proportion and percentage of correct (*not* error) recall were: TYP younger 217/499 = 43%; TYP older 420/733 = 57%; and FXS 216/514 = 42%. Models were trained until they hit this performance level **two** times in a row. Then the average number of epochs need to train was tallied. Originally, we attempted to train the model in the same order that the participants saw the cards, i.e., 1, 2, 3 color only, then 1, 2, 3 color & num. However, the model could not converge and learn the task when the more complex inputs associated with number were suddenly added in the second half of training. We theorized that in the real world children are not presented with the stimuli of colors long before they are exposed to numbers. Both stimuli are present in their environments from a very early age. Thus, it would be appropriate for the model to be trained in the following sequence: 1 color, 1 color & num, 2 color, 2 color & num, 3 color, 3 color & num. The model was able to learn with this sequence of inputs. Because no males with FXS were correct on the foursies, those were not trained for either group.

An epoch represents the entire wave of data for all participants in a particular group (e.g., 1 color, 1 color & num, 2 color, 2 color & num, etc. for all younger TYP participants). In order to assess variability within group models, three separate training models were created with different randomly generated starting seeds. Output comparisons between the three models revealed extremely small Mse differences and so the first model was always retained for further analyses. Analyses were run on an Intel Pentium III with Windows XP OS, 256 MB RAM, 600 MHz speed.

## Modeling Results

### Simulation 1: Younger TYP Model

1) A model was created to simulate how TYP children with an average age of 5.39 (1.06) years would perform on the task. On average this group made 282 errors (out of 499 components, 57%). The training graph in Figure 4 reports errors on the y axis with a dotted line. The model trained to a 282 error rate in four epochs and then hit 282 again at eight epochs, for an average of six epochs of training.

### Simulation 2: Older TYP Model

2) A model was created to simulate how the older TYP children with an average age of 7.60 (2.08) would perform on the task. This group was matched to the males with FXS in reading real words. On average, the older group made 313 errors out of 733 total components (43%). The denominator is higher for this group because the older participant did better on threesies and were able to move into the six trial condition (rather than stopping after three trials). This would also simulate more experience with stimuli in the real world. The older TYP children performed significantly better than the younger TYP children who made 282 errors out of 499 components (57%). Because this is a developmental TYP model, the weights from the first younger model were saved and training resumed on top of those using the older children's data until the proportionally appropriate and smaller error rate of 43% was reached. The model reached these criteria at 17 and again at 19 epochs for an average of 18 epochs of training.

### Simulation 3: FXS model

In numerous articles, Karmiloff-Smith makes the point that changes very early in a developing dynamic system propel learning on a different trajectory. Thus, it was necessary to create a model of an atypical population with a special and different start state. (That is, one cannot train up a TYP model and then lesion it by adding noise as that would simulate an acquired disorder.) FXS is a developmental disorder as it is present in the embryo. There are various methods with which to simulate impairments in models: reducing number of hidden units, randomly changing weights in clean-up mechanisms (Hinton & Shallice, 1991; Hinton, Plaut, & Shallice, 1993), altering the type of training, or eliminating attractor units (Harm & Seidenberg, 1999). Given the architecture of our models and the concept of crisp, distinct phonemic representations, the choice was made to add noise to various internal weight matrices to simulate impairments. The question then became how to distribute the noise across the four chosen levels at the start state?

Noise was applied in a Gaussian distribution over the levels (weight matrices) at two different intensities. These intensities varied by the standard deviation (either .10 or .25). In the first simulation with .25 noise added to all four matrices, the model could not even learn the onesies task after 200 epochs (approximately 24 hours of run time). Training was terminated. Again, males with FXS in this study had an average mental age of over five years and all were able to do some onesies. Clearly, a processing scenario with high noise at all four levels simultaneously did not simulate the functioning of the average male in this study. (Although these sorts of global deficits may exist in individuals who did not qualify for this type of study.)

Table 6 shows performance in terms of number of epochs to train until similar group error rates were reached. A pattern of performance is sought that might reveal mechanisms involved in FXS processing. The main comparisons are between columns three and four (younger vs. FXS model), and columns five and six (older vs. FXS model). Because the males with FXS were quite similar to the younger MA-match TYP children on card task performance, there might be similar amounts of training epochs in the respective columns (i.e., columns three and four). This is seen at the first two levels but at level 3 where time bins are involved, adding a larger amount of noise 'from hidden units to time bins' weights perturbed the system so much that it never converged near 43% correct. This makes sense, upon reflection, because the time bins are iterative and that noise would be run through the system multiple times regressively increasing the dysfunction. Noise is less disruptive when added to level 4 or 'time bins back to hidden units', but it still means that with .25 noise the FXS model would never learn like the older TYP group.

The patterns that would most resemble the current state of FXS functioning in this sample are bolded in Table 6 at levels one and four. At level one, the FXS model displays a similar or eventual match to the TYP- younger processing, and then *never* matches performance in column six (because most males with FXS never did attain the performance of the older TYP matches this is what we would want to see). *Never* means that training was terminated after 200 epochs. A probable match pattern is also seen at level four. Although it took 17 epochs for the FXS model to match the TYP younger group's performance in column three, it eventually made it. At level four with .25 noise, the FXS model never attained the performance of the older TYP-match group.

Given the results of these models, the best choice match patterns between the groups can be seen at the phoneme to hidden units scenario with .25 SD noise, and the time bins to hidden units scenario at .25 SD noise. These patterns lead to two tes table hypotheses that are explicated below.

**Modeling Discussion—**Two TYP models without noise, and several FXS models with noise at various intensities and locations, were created. This is the first phase of our FXS modeling and choices had to be made about model parameters and noise locations. With these four noise locations we were able to test two hypotheses. Future modeling might include noise at other locations (e.g., on the time bin self-projections to further simulate sequential dysfunctions). Because the TYP participants performed significantly different on the Card Task depending on chronological age (which was correlated with mental age and Word ID skills), two separate "end states" were created for the one TYP model. Analyses revealed that the FXS model could always learn with .10 SD noise at various levels - the lesser amount of noise may represent the highest functioning individuals with FXS. The FXS model could never learn a onesie with .25 noise coming from the hidden units to the time bins. In the standard memory model, this would be conceptualized as a problem in the PFC, perhaps with readying information for rehearsal in the phonological loop. In a more emergent memory model, it might be conceptualized as the strength of the refresh signal in the initial activation region. Someone with impairments this severe at that level probably would not make it past the parent phone call screening stage for the study.

The FXS models performed somewhat equivalently to the *younger* TYP models in all other scenarios. Although it did take much longer for the FXS model to train to 43% correct at level 4 with .25 SD noise (17 versus 6 epochs for the younger TYP matches). It is also true that the average FXS participant was four times older - so a case could be made for the extra training.

When .25 SD of noise was added to two levels of interest, the FXS model could not approach the performance of the *older*, better-performing TYP children. This is what we wanted to see, because it resembles the real human data - the FXS males performed significantly worse than the older TYP participants on the onesies, twosies and threesies for color only and they displayed trends for the component counts on the more difficult color and number block. This performance difference between the males with FXS and the older TYP participants implies that even with a substantial age difference favoring the FXS group, their sequential memory skills were not progressing beyond the average level of five and a half-year olds. The models may help to pinpoint where processing weaknesses might reside and guide recommendations for remediation. Two ramifications for phonological processing and sequencing are discussed.

**Phonological ramifications:** The first candidate for a processing deficit may reside at level 1 going from phonemic representations to the hidden units (or central executive). This is the first stage in the phonological loop. We will use the more common language of Baddeley's model in this discussion section, but it is possible to insert more emergent terms like "initial region of activation" for central executive or "reactivation strength" for phono loop. This is an important component in recall - even for visually presented sequential information which is so often recoded verbally (Baddeley, 1986). Smooth functioning in the phonological loop requires that phonemic representations and phonological processing are intact and crisp. Functional phonological processing is also necessary for fluent reading. Reviewing the reading literature reveals that for all individuals, even after partialling out IQ, later reading ability is predicted by phonological processing (Stanovich et al., 1984; Siegel, 1993). The phonological loop is comprised of the representations themselves and their maintenance during rehearsal. First, what does it mean to have distinct representations?

A distinct representations would be crisp and stable; the representation would not unduly degrade as new phonemic input came into the system. Little is known about phonemic representations in males with FXS.[4] However, Johnson-Glenberg (2003;2007a;Buckley & Johnson-Glenberg, 2008) administered The Phonological Awareness Test (PAT: Robertson & Salter, 1997) to six of the final males with FXS in this study. Four relevant subtests were administered: rhyming, segmentation, deletion, and isolation. Only two of the three levels of isolation were examined: initial sound in a CVC word, and final sound (medial was too difficult for this population). The PAT percentile scores for the males with FXS were gathered using the Woodcock-Johnson Word ID age-equivalent score as a base. That is, chronological age was not used because the males with FXS were so much older than the TYP participants and this would have resulted in a meaningless less than 1%ile score across the board. By matching on the ability to read real words, a disconnect between the FXS and TYP groups' skill in using a whole word process or a phonemic assembly process could be examined. Table 7 presents Means and SDs on the Phonological Awareness Test for FXS only. A comparison group of TYP children is not included because it can be assumed from this normed measure that the average TYP child would place in the 50%ile.

Males with FXS consistently score below the 10%ile on these purely phonemic measures. They demonstrate particularly poor skills on the isolation subtest (including an across-the-board failure in this pilot sample to isolate and repeat the middle sound in a CVC word).

The ability to read nonwords is also predictive of phonemic skills and phonological assembly. The Woodcock Johnson Word Attack test was administered to 13 of the males with FXS. Word Attack age equivalent scores were: TYP Word-ID Match= 8.67 (3.43); FXS = 6.45 (1.57), $t_{(25)} = 2.14$, $p=.04$, ES = .91. This t test revels that even though the males with FXS could read *real* words on average like the seven and a half year old TYP children, the males with FXS read *nonwords* significantly lower, equivalent to six and a half year olds. Thus, there is a significant two year lag when comparing nonword reading. These PAT test pilot data demonstrate a weakness at the phonemic representational level and the nonword (Word Attack) scores demonstrate a dissociation at the word and assembly levels of phonological processing. Thus, a network that had higher levels of noise or imprecision at both levels 1 (phoneme to hidden) and 4 (time sequencing back to hidden) would be a good candidate for a model of males with FXS.

**Sequencing ramifications:** The Conners' et al. (2001) result with a group of individuals with ID found that refreshing the phonological loop was predictive of relative decoding skill. The level 4 pattern in Table 6 that matched the FXS and TYP performances also implicates sequencing and retrieval problems for those with FXS. Adding .25 SD noise to the connections projecting from time bins back to the hidden units (Central Executive) matched the younger TYP performance after 17 epochs of training; however, FXS model performance never reached the level of accuracy attained by the older TYP participants- which is what we would expect. The location of these connections could implicate the internal time signal which is assumed to be located in the basal ganglia (O'Reilly & Frank, 2005).

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[4] In the expressive arena of phonology, Roberts, Hennon, and Anderson (2003) report that males with FXS have expressive difficulty with consonant substitutions, omissions and distortions which are characteristic of developmentally younger children.

A faulty or imprecise timing signal would explain many of the sequencing deficits in this population and is supported by the across-the-board sequencing deficits seen in this entire study where the younger TYP MA-match group outperformed the males with FXS on all the sequencing memory measures including: Verbal Auditory Learning (VAL-verbal immediate and delayed versions), and KABC hand movements (nonverbal immediate). An imprecise signal from the timing mechanism may explain compromised performance during recall of ordered items. Working memory deficits have also been observed in females with FXS. Greicius, Boyett-Anderson, Menon and Reiss' (2004) fMRI study revealed that females with FXS displayed significantly less activation in the hippocampus and basal forebrain in a test of visual memory encoding when compared to TYP chronological age-matches.

**Future modeling and research:** There are numerous variations of architecture, noise and/or ablation that could be performed on the FXS models. Due to space and theory constraints only four variations (deemed the best candidates) for FXS processing have been presented. Future research could include sensitivity analyses wherein one or more input vectors have systematic, yet disproportionate, amounts of activation added. After training, analyses would follow how these activations perturbate through the system and reveal which connections are the primary predictors of performance. In addition, cluster analyses or multidimensional scaling techniques could then be used to observe how the weight matrices aggregate at various training stages. These might further reveal how the phonological, lexical, and timing levels interact in a developmental manner.

Roberts et al. (2003) report oral motor difficulties for males with FXS when repeating multisyllablic sequences and postulate motor planning problems with this population. Motor planning is a level that should be included in future models. In addition, males with FXS present with hyperarousal problems. Miller et al. (1999) describe a series of experiments that demonstrate that the electrodermal responses (EDRs) of individuals with FXS are significantly different from those of normal controls in regards to stimulation of the five sensory systems. This ongoing vigilance for, and attention to, new information and the inability to compress and accommodate information in long term store (learning), may also explain some of the anxiety observed in individuals with FXS. A future addition to a more complex model of cognition for these individuals might include more thoughtful hippocampal-type processing. At the cellular level, abnormal dendritic spine structures have been observed both in humans and in FMRP knock-out mice hippocampi (Irwin, Galvez, & Greenough, 2000a).

Due to resource constraints, funds were not available for precise genetic testing or the administration of an autism screening test. Future research might address the comorbidity between FXS and autism and analyze if there are memory differences between these populations. There is some consensus regarding a 25% to 30% prevalence of "autism" in FXS (Bailey et al., 2004). However, considerable controversy surrounds this topic. When a subgroup distinction is made, we prefer the term "individuals with FXS and autism-like symptoms". The definition of Autism Spectrum Disorder is extremely broad (think of the difference between highly verbal individuals with Asperger's syndrome and those with PDD-NOS and no verbal language at all). In addition, there is an ongoing debate regarding the underlying mechanisms responsible for behaviors (Lewis, et al. 2006), these may not be the same in those with FXS and those with idiopathic autism. That is, the symptomology may match, e.g., eye gaze aversion, but in the males with FXS such avoidance may be primarily due to anxiety.

**Application and remediation:** If more training time had been allotted to the more damaged FXS models would they have eventually resembled the older TYP models? Depending on the level where the noise had been added, sometimes *more* training resulted in *less* accuracy over time- which is one reason why a 200 epoch (24 hour) cut-off was chosen. This suggests that if the trajectory goes so far astray in the beginning then such systems are not self-correcting.

This finding should not be used to suggest that there are certain critical “windows” wherein an affected individual must receive intervention. It is our contention that it is never too late to apply thoughtful intervention. We did not model the process of intervention; this would be an excellent future research question to model.

Without question, interventions need to be more research-based. These neural network models suggest two levels of processing that might benefit from targeted intervention: phonological and sequential processing. How would adding a remediation aimed at the phonological level affect performance (of both humans and computational models)? At this time, there is no research on training explicit phonological awareness techniques to males with FXS. Perhaps with intense, one-on-one tutoring in phonological awareness, the noise associated with the connections from phonemes to hidden units would be attenuated. An appropriate intervention comparison group would be one that was receiving a more whole word training method. Anecdotally, this appears to be the standard in the schools as reported by parents, and as revealed by reviews of commercialized reading programs for those with ID. Recommendations are strongly made for more phonological awareness training for this population so they can learn how to sound out novel words and are given access to the tools necessary to grow as more independent readers. Research on individuals with dyslexia shows that training explicitly in phonemic and phonological awareness generally increases performance on real and nonword reading skills (Clark & Uhry 1995; Olson, Wise, Johnson, & Ring, 1997). In addition, for K-2nd grade children bi-directional relations have been observed between phonological processing and reading-related knowledge, i.e., phonological processing abilities exert strong causal influences on decoding, and letter-name knowledge exerts a more modest causal influence on subsequent phonological processing abilities (Wagner, Torgesen, & Rashotte, 1994).

Sequencing also appears to be a weakness in this population. Because the brain is so plastic, all activities that promote sequencing should be encouraged in home and school settings. In addition, it may also be beneficial to train in strategies. The observation that individuals performed better on the Card Task when they subvocalized would suggest teaching individuals with ID explicit strategies, e.g., the strategy to verbally mediate hand movements or other sequences. Using a verbal cue to perform a physical task may have applications in the life skills sector, as well. In terms of modeling, use of strategies may have the effect of removing or attenuating noise from the signal. By adding an additional mode, e.g., verbalizing - to the processing, the signal may be effectively boosted.

**Conclusions:** This article represents an “enterprise” endeavor designed to 1) create a framework of memory skills in males with FXS, 2) computationally model a verbal sequential working memory task, and 3) craft suggestions regarding appropriate remediations for weaker processing areas. The memory framework is still in its early stages, but a clearer picture is beginning to emerge in regards to the immediate and delayed memory functions in the population of males with FXS. This knowledge can be used to design more appropriate remediation programs that take into account how poor phonemic awareness, compromised sequencing, and attenuated delayed memory functions affect learning. If it is true that memory and learning rely on the facile interleaving of new and old information (McClelland & Goddard, 1996), then creative solutions must be sought at various levels for those with FXS. Some of these levels include: 1) how old information can be more stably and meaningfully encoded, 2) how new information can be presented in a more distributed manner for better integration, 3) how new information can be presented with special emphasis on the components that will overlap with older, long term information - *interleaving facilitation*, and 4) how mastery levels should be more thoughtfully conceived (e.g., is 80% correct three times in a row considered mastery for this population- will that guarantee transfer?).

Modeling is important to help reify conceptualizations of deficits in developmentally disabled populations and to suggest more cognitively valid guidelines for instruction. These models suggest that strong candidates for verbal memory sequencing deficits exist at the encoding and sequencing levels for males with FXS. It should also be noted that no individual (or model) in this article is considered to be at the “end state”. In the developmental vernacular, it would be inappropriate to take the term end state literally. The individual has not reached the end of learning even when tested at 38 years of age (the oldest participant in this study). Johnson-Glenberg and Chapman (2004) encouraged teachers and caregivers of children with Down syndrome to continue increasing and stimulating their children’s vocabulary into adulthood. Encouragement should be given to those who work with individuals with FXS to provide intervention directed toward increasing strategy use, confirming distinct phonological representations, enhancing sequencing skills, and encouraging reading skills throughout the lifespan.

## References

Abbeduto L, Evans J, Dolan T. Theoretical perspectives on language and communication problems in mental retardation and developmental disabilities. Mental Retardation and Developmental Disabilities Research Reviews 2001;7:45–55. [PubMed: 11241882]

Abbeduto L, Murphy M, Cawthon S, Kesin E, Weissman MD, Karadottir S, O’Brien A. Receptive language skills of adolescents and young adults with mental retardation: A comparison of Down syndrome and fragile X syndrome. American Journal on Mental Retardation 2003;108:149–160. [PubMed: 12691594]

Atkinson, RC.; Shiffrin, RM. Human memory: A proposed system and its control processes. In: Spence, KW.; Spence, JT., editors. Psychology of learning and motivation: II. Academic Press; Oxford: 1968. p. 162-181.

Baddeley, A. Working Memory. Oxford University Press; Oxford, England: 1986.

Bailey, DB.; Roberts, JE.; Hooper, SR.; Hatton, DD.; Mirrett, PL.; Roberts, JE.; Schaaf, JM. Research on fragile X syndrome and autism: Implications for the study of genes, environments, and developmental language disorders. In: Rice, ML.; Warren, SF., editors. Developmental Language Disorders: From Phenotypes to Etiologies. Lawrence Erlbaum; Mahwah, NJ: 2004. p. 121-150.

Barsalou LW, Simmons WK, Barbey AK, Wilson CD. Grounding conceptual knowledge in modality-specific systems. Trends in Cognitive Science 2003;17(2):80–91.

Belmont, JM.; Butterfield, EC. The relations of short term memory to development and intelligence. In: Lipsitt, LC.; Reese, HW., editors. Advances in child development and behavior: Vol. 4. Academic Press; New York: 1969.

Buckley, S.; Johnson-Glenberg, MC. Increasing literacy learning for individuals with Down syndrome and fragile X syndrome. In: Warren, SF.; Fey, ME.; Roberts, JE.; Chapman, RS.; Warren, SF., editors. Communication and language intervention series: Speech and language development and intervention in Down syndrome and fragile X syndrome. Paul H. Brookes Publishing Co; Baltimore: 2008. p. 233-254.

Burgess N, Hitch GJ. Memory for serial order: A network model of the phonological loop and its timing. Psychological Review 1999;106(3):551–581.

Campione, JC.; Brown, AL. Memory and metamemory development in educable retarded children. In: Kail, RV., Jr.; Hagen, WJ., editors. Perspectives on the Development of Memory and Cognition. Erlbaum; Mahwah, NJ: 1977. p. 367-406.

Carrow-Woolfolk, E. Test for Auditory Comprehension of Language- Revised. DLM Teaching Resources; Allen, TX: 1985.

Chapman RS. Children’s language learning: An interactionist perspective. Journal of Child Psychology and Psychiatry and Allied Disciplines 2000;41(1):33–54.

Clark, DB.; Uhry, JK. Dyslexia: Theory and Practice of Remedial Instruction. York Press; Baltimore, MD: 1995.

Cohen IL. An artificial neural network analogue of learning in autism. Biological Psychiatry 1994;36:5–20. [PubMed: 8080903]

Conners FA, Atwell JA, Rosenquist CJ, Sligh AC. Abilities underlying decoding differences in children with intellectual disability. Journal of Intellectual Disability Research 2001;45(4):292–299. [PubMed: 11489050]

Cornish KM, Turk J, Wilding J, Sudhalter V, Munir F, Kooy F, Hagerman R. Deconstructing the attention deficit in fragile X syndrome: A developmental neuropsychological approach. Journal of Child Psychology and Psychiatry 2004;45(6):1042–1053. [PubMed: 15257661]

Cowan, NT. The development of working memory. In: Cowan, Nelson T., editor. The Development of memory in childhood. Psychology Press; Sussex UK: 1997. p. 163-199.

Crosby KG. Attention and distractibility in mentally retarded and intellectually average children. American Journal of Mental Deficiency 1972;77(1):46–53. [PubMed: 5052426]

D'Esposito M, Postle BR, Rypma B. Prefrontal cortical contributions to working memory: Evidence from event-related fMRI studies. Experimental Brain Research 2000;133(1):3–11.

Dempster FN. Memory span: Sources of developmental and individual differences. Psychological Bulletin 1981;89:63–100.

Dykens EM, Hodapp RM, Leckman JF. Strengths and weaknesses in the intellectual functioning of males with fragile X syndrome. American Journal of Medical Genetics 1987;28:13–15. [PubMed: 3674106]

Ehri, LC. Reconceptualizing the development of sight word reading and its relation to decoding. In: Gough, PB.; Ehri, LC.; Treiman, R., editors. Reading Acquisition. LEA; Hillsdale, NJ: 1992. p. 324-344.

Elbro C, Borstrom I, Petersen DK. Predicting Dyslexia from kindergarten: The importance of distinctness of phonological representations of lexical items. Reading Research Quarterly 1998;33(1):36–60.

Ellis, NR. Memory processes in retardates and normals. In: Ellis, NR., editor. International review of research in mental retardation: Vol. 4. Academic Press; New York: 1963.

Elman JL. Finding structure in time. Cognitive Science 1990;14:179–211.

French J, Worcester DA. Critical study of the Columbia Mental Maturity Scale. Exceptional Children 1956;23:111–113.

Freund LS, Reiss AL. Cognitive profiles associated with fra(X) syndrome in males and females. American Journal of Medical Genetics 1991;38:542–547. [PubMed: 2063895]

Glenberg AM, Kaschak MP. Grounding Language in Action. Psychonomic Bulletin & Review 2002;9 (3):558–565. [PubMed: 12412897]

Gluck, MA.; Myers, CE. Gateway to Memory: An Introduction to Neural Network Modeling of the Hippocampus and Learning. MIT Press; Cambridge, MA: 2001.

Greicius MD, Boyett-Anderson JM, Menon V, Reiss AL. Reduced basal forebrain and hippocampal activation during memory encoding in girls with fragile X syndrome. Neuroreport 2004;15(10): 1579–1584. [PubMed: 15232287]

Gustafsson L. Inadequate cortical feature maps: A neural circuit theory of autism. Biological Psychiatry 1997;42:1138–1147. [PubMed: 9426884]

Hagerman, RJ. Neurodevelopmental Disorders. Oxford University Press; Oxford: 1999.

Harm MW, Seidenberg MS. Phonology, acquisition, and dyslexia: Insights from connectionist models. Psychological Review 1999;106(3):491–528. [PubMed: 10467896]

Hinton GE, Plaut DC, Shallice T. Simulating Brain Damage. Scientific American 1993;(October):76–82. [PubMed: 8235551]

Hinton GE, Shallice T. Lesioning an attractor network: Investigations of acquired dyslexia. Psychological Review 1991;98(1):74–95. [PubMed: 2006233]

Hodapp RM, Leckman JF, Dykens EM, Sparrow S, Zelinsky D, Ort S. KABC profiles in children with fragile X syndrome, Down syndrome and nonspecific mental retardation. American Journal on Mental Retardation 1992;97:39–36. [PubMed: 1386742]

Howieson, DB.; Lezak, MD. Separating memory from other cognitive problems. In: Baddeley, AD.; Wilson, BA.; Watts, FN., editors. Handbook of Memory Disorders. John Wiley & Sons; Oxford: 1995. p. 411-426.

Irwin SA, Galvez R, Greenough WT. Dendritic spine structural anomalies in fragile X mental retardation syndrome. Cerebral Cortex 2000a;10:1038–1044. [PubMed: 11007554]

Jensen O, Lisman JE. An oscillatory short-term memory buffer model can account for data on the Sternberg Task. The Journal of Neuroscience 1998;18(24):10688–10699. [PubMed: 9852604]

Johnson-Glenberg, MC. Society for Research on Children's Language Disorders (SRCLD). 2003. Literacy and working memory in those with fragile X syndrome.

Johnson-Glenberg, MC. Fragile X syndrome: Memory skills and the emergence of reading in males. In: Paul, R., editor. Language Disorders from a developmental perspective: Essays in honor of Robin Chapman. LEA; Mahwah, NJ: 2007a. p. 215-247.

Johnson-Glenberg MC, Chapman RS. Predictors of parent-child language during novel task play: A comparison between typically developing children and individuals with Down syndrome. Journal of Intellectual Disability Research 2004;48(3):225–238. [PubMed: 15025665]

Karmiloff-Smith, A.; Thomas, MS. Developmental disorders. In: Arbib, MA., editor. The handbook of brain theory and neural networks. Vol. 2nd. MIT Press; Cambridge, MA: 2002. p. 292-294.

Kaufmann WE, Abrams MT, Chen W, Reiss AL. Genotype, molecular phenotype, and cognitive phenotype: Correlations in fragile X syndrome. American Journal of Medical Genetics 1999;83:286–295. [PubMed: 10208163]

Kaufman, AS.; Kaufman, NL. Kaufman Assessment Battery for Children - Interpretive Manual. AGS; Circle Pines, MN: 1983.

Levy W. A sequence predicting CA3 is a flexible associator that learns and uses context to solve hippocampal-like tasks. Hippocampus 1996;6:579–590. [PubMed: 9034847]

Lewis P, Abbeduto L, Murphy M, Richmond E, Giles N, Bruno L, Schroeder S. Cognitive, language and social-cognitive skills of individuals with fragile X syndrome with and without autism. Journal of Intellectual Disability Research 2006;50(7):532–545. [PubMed: 16774638]

Mazzocco, M.; Reiss, AL. Behavioral Neurogenetics Approach to Understanding the Fragile X syndrome. In: Tager-Flusberg, H., editor. Neurodevelopmental Disorders: Contributions to a New Framework from Cognitive Neurosciences. 1999. p. 43-63.

McClelland JL, Goddard NH. Considerations arising from a complementary learning systems perspective on hippocampus and neocortex. Hippocampus 1996;6:654–665. [PubMed: 9034852]

McClelland JL, McNaughton BL, O'Reilly RC. Why there are complementary learning systems in the hippocampus and neocortex: Insights from the successes and failures of connectionist models of learning and memory. Psychological Review 1995;102(3):419–457. [PubMed: 7624455]

Miles S, Chapman RS. Narrative content as described by individuals with Down syndrome and typically developing children. Journal of Speech, Language, and Hearing Research 2002;45:175–189.

Miller LJ, McIntosh DN, McGrath J, Shyu V, Lampe M, Taylor AK, Tassone F, Neitzel K, Stackhouse T, Hagerman RJ. Electrodermal responses to sensory stimuli in individuals with fra(X). A preliminary report. American Journal of Medical Genetics 1999;83:268–279. [PubMed: 10208160]

Miyake A, Friedman NP, Emerson MJ, Witzki AH, Howerter A, Wager TD. Contributions to complex "Frontal Lobe" tasks: A latent variable analysis. Cognitive Psychology 2000;41:49–100. [PubMed: 10945922]

Munir F, Cornish KM, Wilding J. Nature of the working memory deficit in fragile-X syndrome. Brain and Cognition 2000;44:387–401. [PubMed: 11104532]

Oberle I, Rousseau F, Heitz D, Kretz C, Devy's D, Hanauer A, Boue J, et al. Instability of a 550-base pair DNA segment and abnormal methylation in fragile X syndrome. Science 1991;252:1097–1102.

Olson, RK.; Wise, BW.; Johnson, MC.; Ring, J. The etiology and remediation of phonologically based word recognition and spelling disabilities: Are phonological deficits the "hole" story. In: Blachman, B., editor. Foundations of Reading Acquisition. Lawrence Erlbaum, Inc.; Mahwah, NJ: 1997. p. 305-326.

O'Reilly, RC.; Busby, RS.; Soto, R. Three forms of binding and their neural substrates: Alternatives to temporal synchrony. In: Cleeremans, A., editor. The Unity of Consciousness: Binding, Integration, and Dissociation. Oxford University Press; Oxford: 2003. p. 168-192.

O'Reilly RC, Frank MJ. Making working memory work: A computational model of learning in the prefrontal cortex and basal ganglia. Neural Computation 2005;18:283–328.

O'Reilly, RC.; Munakata, Y. Computational Explorations in Cognitive Neuroscience: Understanding the Mind by Simulating the Brain. MIT Press; Cambridge, MA: 2000.

O'Reilly, RC.; Soto, R. A model of the phonological loop: Generalization and binding. In: Dietterich, TG.; Becker, S.; Ghahramani, Z., editors. Advances in Neural Information Processing Systems (NIPS) 14. MIT Press; Cambridge, MA: 2002.

Plaut DC, McClelland JL, Seidenberg MS, Patterson K. Understanding normal and impaired reading: Computational principles in quasi-regular domains. Psychological Review 1996;103:56–116. [PubMed: 8650300]

Postle BR. Working memory as an emergent property of mind and brain. Neuroscience 2006;139(1):23–38. [PubMed: 16324795]

Pugh KR, Mencel WE, Jenner AR, Katz L, Frost SJ, Lee JR, Shaywitz SE, Shaywitz BA. Neurobiological studies of reading and reading disability. Journal of Communication Disorders 2001;34:479–492. [PubMed: 11725860]

Reiss AL, Freund LS. Fragile X syndrome, DSM-III-R, and autism. Journal of the American Academy of Child and Adolescent Psychiatry 1990;29:885–891. [PubMed: 2273015]

Roberts J, Hennon EA, Anderson K. Fragile X syndrome and speech and language. The ASHA Leader 2003;8(19):6–10.

Robertson, C.; Salter, W. The Phonological Awareness Test. LinguiSystems Inc.; East Moline, IL: 1997.

Schacter, DL.; Tulving, E. Memory Systems 1994. MIT Press; Cambridge, MA: 1994.

Scharfenaker, S.; O'Connor, R.; Stackhouse, T.; Braden, M.; Hickman, L.; Gray, K. An integrated approach to intervention. In: Hagerman, R.; Cronister, A., editors. Fragile X syndrome: Diagnosis Treatment and Research. Johns Hopkins Press; Baltimore MD: 1996. p. 349-411.

Scott SK, Blank CC, Rosen S, Wise RJS. Identification of a pathway for intelligible speech in the left temporal lobe. Brain 2000;123(12):2400–2406. [PubMed: 11099443]

Shaywitz SE, Shaywitz BA. Dyslexia (specific reading disability). Biological Psychiatry 2005;57:1301–1309. [PubMed: 15950002]

Siok WT, Jin Z, Flecher P, Tan LH. Distinct brain regions associated with syllable and phoneme. Human Brain Mapping 2003;18(3):201–207. [PubMed: 12599278]

Seidenberg M, McClelland J. A distributed developmental model of word recognition and naming. Psychological Review 1989;96:523–568. [PubMed: 2798649]

Siegel LS. Phonological processing deficits as the basis of a reading disability. Developmental Review 1993;13:246–257.

Smith ML, Milner B. The role of the right hippocampus in the recall of spatial location. Neuropsychologia 1981;19(6):781–793. [PubMed: 7329524]

Sobesky, WE.; Hull, CE.; Hagerman, RJ. The emotional phenotype in mildly affected carriers. In: Hagerman, RJ.; McKenzie, P., editors. 1992 International Fragile X Conference Proceedings; Spectra/National fragile X foundation: Denver. 1992. p. 99-106.

Stanovich KE, Cunningham AE, Feeman DJ. Intelligence, cognitive skills and early reading progress. Reading Research Quarterly 1984;19:278–303.

Strand S, Deary I, Smith P. Sex differences in cognitive abilities test scores: A UK national picture. British Journal of Educational Pschology 2006;76(3):463–480.

Squire, LR.; Knowlton, BJ. The medial temporal lobe, the hippocampus, and the memeory systems of the brain. In: Gazzaniga, MS., editor. The New Cognitive Neurosciences. MIT Press; Cambridge, MA: 2000. p. 765-780.

Thelen, E. A Dynamic Systems Approach to the Development of Cognition and Action. MIT Press; Cambridge, MA: 1994.

Thomas MS, Karmiloff-Smith A. Modelling language acquisition in atypical phenotypes. Psychological Review 2003;110(4):647–682. [PubMed: 14599237]

Thorndike, RL.; Hagen, EP.; Sattler, JM. Stanford-Binet Intelligence Scale: Fourth edition. Riverside; Chicago: 1986.

Ullman MT. Contributions of memory circuits to language: The declarative/procedural model. Cognition 2004;92:231–270. [PubMed: 15037131]

Verkerk AJ, Pieretti M, Sutliffe JS, Fu YH, Kuhl DP, Pizutti A, Reiner O, et al. Identification of a gene (FMR-1) containing a CGG repeat coincident with a breakpoint cluster region exhibiting length variation in fragile X syndrome. Cell 1991;65:905–914. [PubMed: 1710175]

Wagner RK, Torgesen J,K, Rashotte C. Development of reading-related phonological processing abilities: New evidence of bidirectional causality from a latent variable longitudinal study. Developmental Psychology 1994;30(1):73–87.

Weiss B, Weisz JR, Bromfield R. Performance of retarded and nonretarded persons on information-processing tasks: Further tests of the similar structure hypothesis. Psychological Bulletin 1986;100 (2):157–175. [PubMed: 3763783]

Woodcock, RW. Woodcock Reading Mastery Tests - Revised. AGS; Circle Pines, MN: 1998.

Woodcock, RW.; McGrew, KS.; Mather, N. Woodcock-Johnson Tests of Cognitive Abilities. Riverside Publishing; Rolling Meadows, IL: 2001.

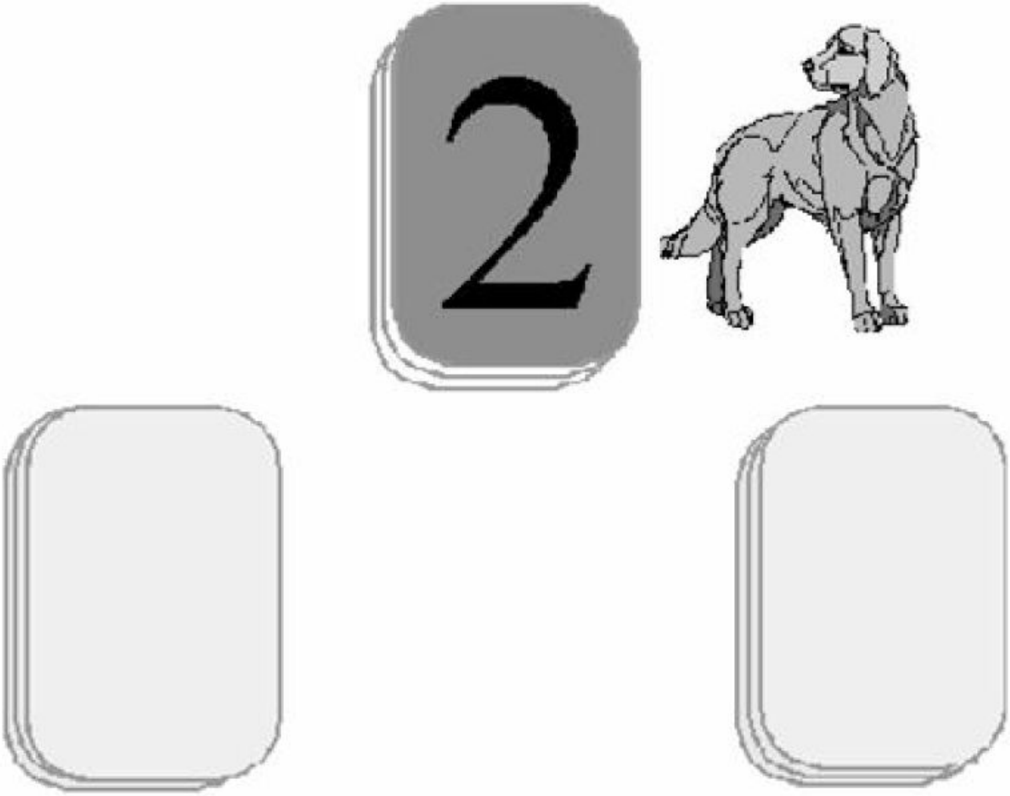


**Figure 1.**
Example of Card Task screen.

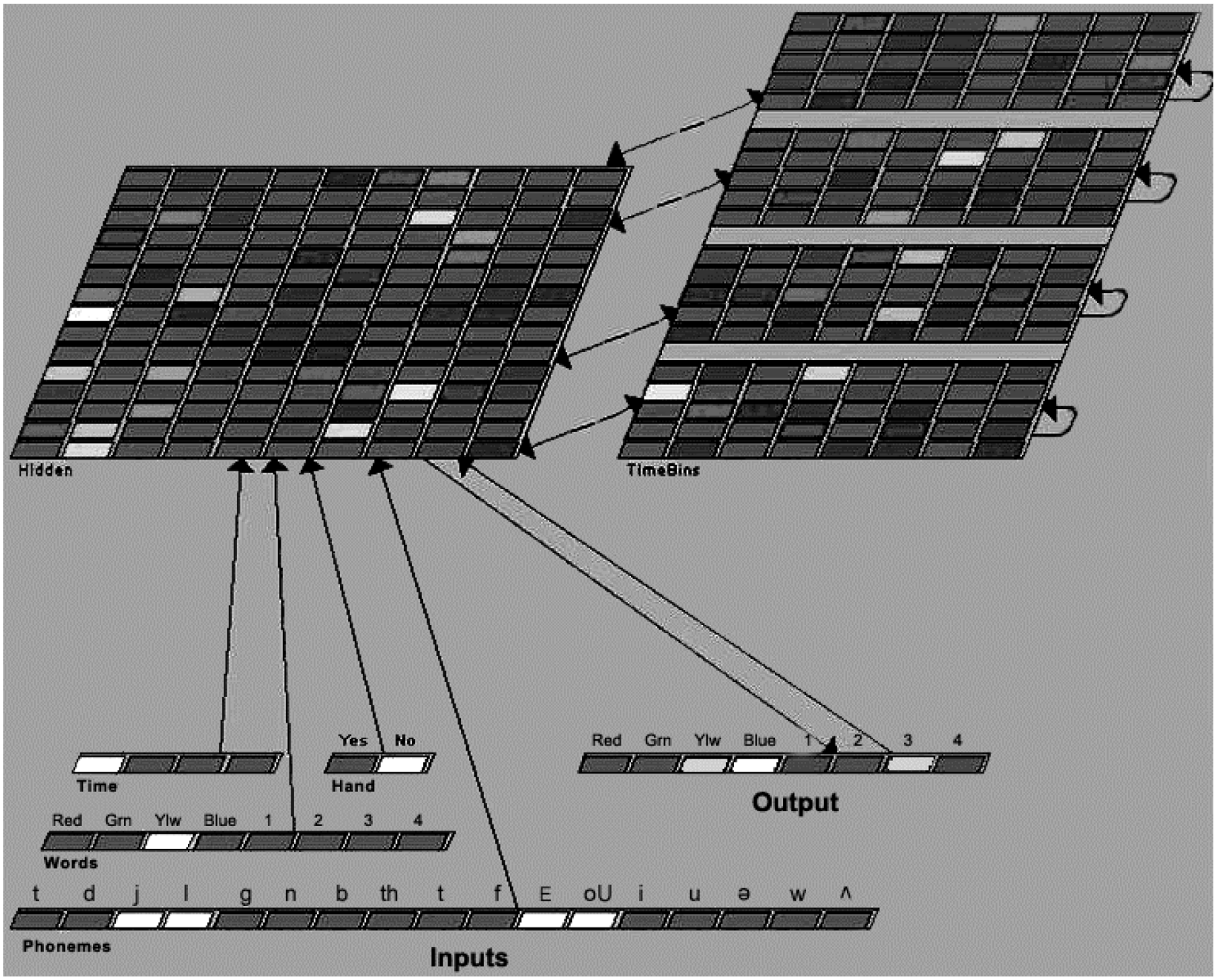
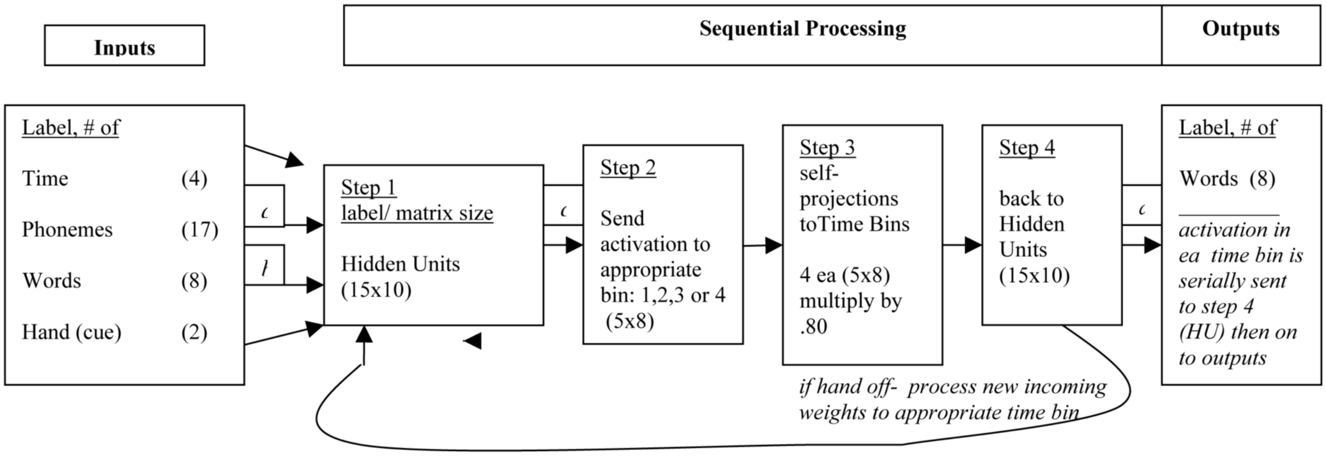


**Figure 2.**
The neural network model for the Card Task.



note. *a, b, c,* and *d* represent the 'levels' or weight matrices where noise will be added.

**Figure 3.**

Schematic of the steps in the neural network model of the Card Task.

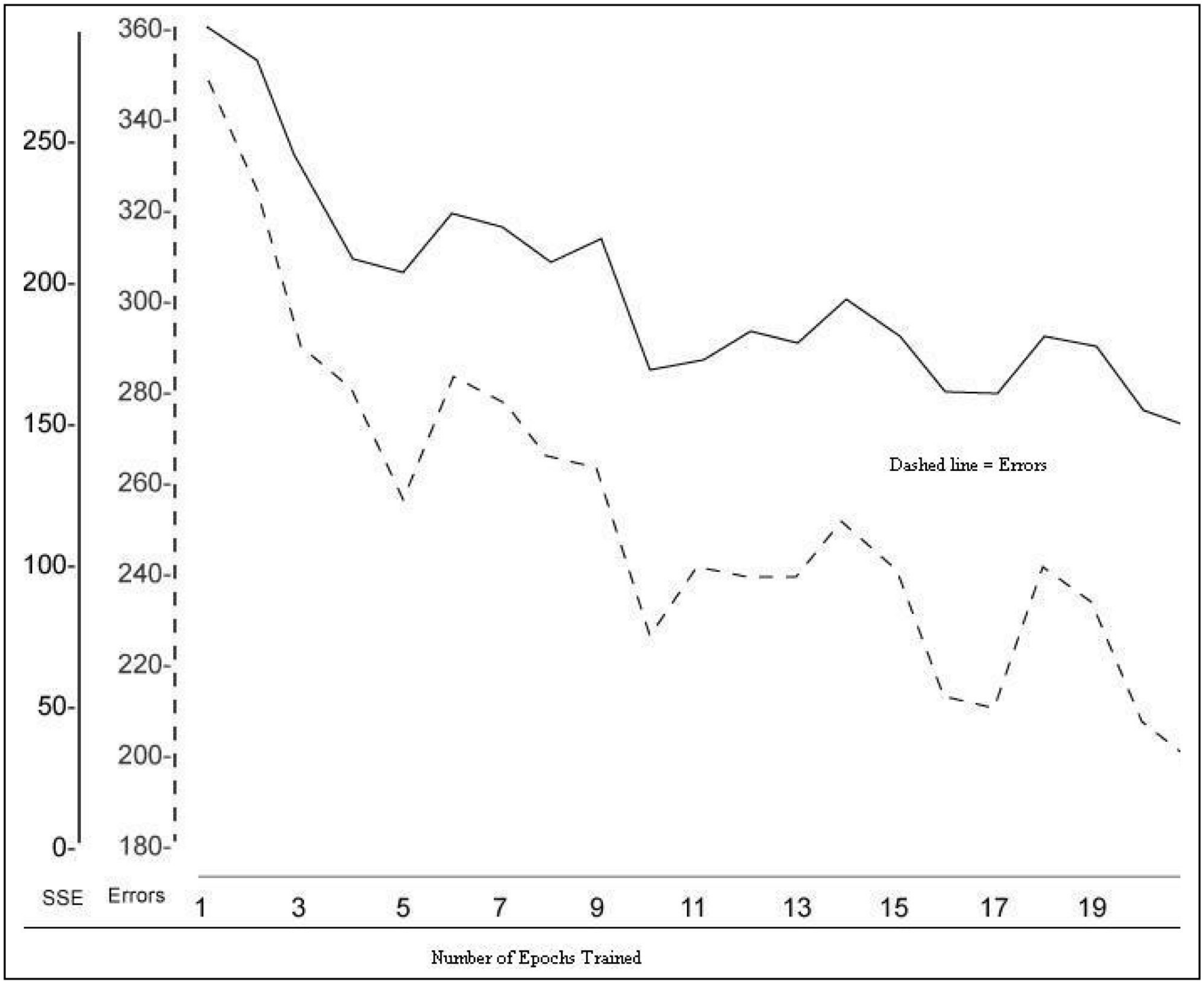


**Figure 4.**
Errors per epochs of training for the typically developing (TYP) network model.

## Table 1

The Memory Framework with Predicted Favored Groups

| **Time and Mode** | **Processing-More Simultaneous** | **Processing-More Sequential** |
|---|---|---|
| Verbal Immediate | **FXS** | TYP |
| Verbal Delayed | TYP | TYP |
| NonVerbal Immediate | **FXS** | TYP |
| NonVerbal Delayed | TYP | ** no measures avail. at time** |

## Table 2

Match Variables and t-tests Between FXS and TYP Groups

| | **FXS**<br>**M (SD)** | **TYP-MA**<br>**M (SD)** | **t test to FXS** | **TYP-Word ID**<br>**M (SD)** | **t-test to FXS** |
|---|---|---|---|---|---|
| N | 15 | 22 | | 13 | |
| Nonverbal Mental Age (Standford Binet) | 5.30 (1.26) | 5.73 (1.13) | ≤ 1.0 | 8.71 (3.94) | $t_{(15)}{}^{a} = 3.03$, $p = .008$ |
| Word Identification (Woodcock- Johnson) | | | | | |
| Raw Score | 36.80 (23.16) | 14.83 (23.24) | $t_{(18)} = 2.12$, $p = .048$ | 41.15 (33.84) | ≤ 1.0 |
| Age Equivalent | 8.00 ( 1.34) | 5.97( 1.51) | $t_{(18)} = 2.99$, $p = .008$ | 8.08 ( 2.63) | ≤ 1.0 |

Notes.

[a] = Where variance between groups differed significantly, degrees of freedom have been adjusted.

## Table 3

Results Comparing FXS and MA-matched Group with Effect Sizes and Favored Group (if Difference is a Trend or Better)

| **Measure** | **TD MA-Match M (SD)** | **FXS M (SD)** | **t-test** | ***p*** | **ES** | **Favored Group** |
|---|---|---|---|---|---|---|
| **Verbal Immediate—Spatial**<br>Toy Recall I<br>Card Task — Onesies % | 6.09 (1.70)<br>57.88 (24.41) | 8.25 ( 3.41)<br>56.67 (35.94) | $t_{(21)} = 1.89$<br>t<1.0 | .07 | .84 | FXS |
| **Verbal Immediate-Sequent**.<br>VAL — error count<br>Card Task — Twosies %<br>Card Task — Threesies % | 32.60 (11.24)<br>28.47 (22.24)<br>3.12 (8.54) | 50.71 (23.70)<br>24.40 (22.35)<br>1.17 (4.38) | $t_{(19.6)} = 2.23$<br>t<1.0<br>t<1.0 | .04 | 1.04 | **TD** |
| **Verbal Delayed—Spatial**<br>Toy Recall II | 4.63 ( 2.61) | 5.92 (2.02) | $t_{(18)} = 1.25$ | | .56 | |
| **Verbal Delayed-Sequent.**<br>VAL II—Delay-error | 28.67 (6.69) | 49.43 (19.71) | $t_{(17.2)} = 3.63$ | .002 | .79 | **TD** |
| **NonVerbal Immed.—Spatial**<br>Gestalt Mem (recog)—raw | 12.60 (3.86) | 18.07 (3.35) | $t_{(21)} = 3.64$ | .002 | 1.52 | **FXS** |
| **NonVerbal Immed.-Sequent**.<br>Hand Movements-Raw | 6.55 ( 2.46) | 3.00 (2.16) | $t_{(22)} = 3.75$ | .001 | 1.54 | **TD** |
| **NonVerbal Delayed-Spatial**<br>Toy Placement, Mean cm | 14.26 (4.47) | 18.07 (7.85) | $t_{(22)} = 1.42$ | | .62 | |

*Note*. When variances are significantly unequal, the degrees of freedom are adjusted and contain a decimal place.

## Table 4

Memory Tasks by Time, Mode and Processing - Significant Group is Bolded and Underlined

| **Time and Mode** | **Processing- More Simultaneous/Spatial** | **Processing- More Sequential** |
|---|---|---|
| Verbal Immediate | Toy Recall FXS>TYP<br>Card Task (Onesies) FXS=TYP | Card Task (Twosies, Threesies- *WORD-ID match*) FXS<**TYP**<br>Verbal Auditory Learning (VAL) FXS<**TYP** |
| Verbal Delayed | Toy Recall (delay) FXS<TYP | Verbal Auditory Learning (VAL-delay) FXS<**TYP** |
| NonVerbal Immediate | Gestalt Memory **FXS**>TYP | Hand Movements FXS<**TYP** |
| NonVerbal Delayed | Toy Placement (delay) FXS=TYP | |

## Table 5

Percent Correct and t-tests on Card Task with WordID Match Group

| Card Task | WordID-TYP | FXS | t test | *p* | N |
|---|---|---|---|---|---|
| **COLOR ONLY** | | | | | On avg.<br>TD= 13<br>FX= 15 |
| Onesies (4 trials) | 82.69 (21.37) | 50.00 (36.59) | $t_{(26)} = 2.83$ | .009 | |
| Twosies (6 trials) | 51.15 (24.69) | 22.20 (23.06) | $t_{(26)} = 3.21$ | .004 | |
| Twosies-components Max. 12 | 66.69 (18.88) | 45.07 (20.72) | $t_{(26)} = 2.87$ | .008 | |
| Threesies (3 or 6 trials) | 18.75 (26.05) | 1.17 ( 4.38) | $t_{(11.5)} = 2.31$ | .040 | |
| Threesies-components Max. 9 or 18 | 45.25 ( 25.11) | 25.58 (21.69) | $t_{(22)} = 2.05$ | .052 | |
| **COLOR & NUMBER** | | | | | |
| Onesies (4 trials) | 64.58 (34.47) | 44.64 (32.79) | $t_{(24)} = 1.51$ | | |
| Onesie-components Max. 8 | 78.25 (24.55) | 57.85 (31.37) | $t_{(22)}=.1.77$ | .090 | |
| Twosies (6 trials) | 23.67 (35.07) | 6.46 (10.85) | $t_{(12.9)} = 1.63$ | | |
| Twosies- components Max. 24 | 58.42 (23.88) | 33.77 (18.39) | $t_{(22)} = 2.83$ | .010 | |
| Threesies (3 or 6 trials) | 5.00 (11.19) | .00 (.00) | $t_{(12)} = 1.41$ | | TD = 10<br>FX = 4 |
| Threesies-components Max.18 or 36 | 48.60 (18.05) | 29.75 (14.45) | $t_{(12)} = 1.85$ | .089 | TD = 10<br>FX = 4 |

## Table 6

Epochs to Train: Level Location x Noise Amount x Model

| Level Location of Noise in FXS model | SD of Noise in FXS model | Epochs - TD Younger (MA-Match 43% correct) Took approx. | Epochs - FXS model took: | Epochs - TD Older (Word-ID Match 57% correct) Took approx. | Epochs - FXS model took: |
|---|---|---|---|---|---|
| **1) Phoneme to Hidden** | **.25** | **6** | **5** | 18 | **never**[a] |
| | .10 | 6 | 7 | 18 | 24 |
| 2) Word to Hidden | .25 | 6 | 6 | 18 | 30 |
| | .10 | 6 | 5 | 18 | 29 |
| 3) Hidden to Time Bins | .25 | 6 | never[a] | 18 | never[a] |
| | .10 | 6 | 8 | 18 | 34 |
| **4) Time Bins back to Hidden** | **.25** | **6** | **17** | 18 | **never**[a] |
| | .10 | 6 | 7 | 18 | 31 |

Notes.

**Bolded cells** represent best contenders for current model of deficit in males with FXS.

[a] connotes that the model did not converge after 200 epochs and training was terminated.

## Table 7

Means and SDs for the Phonological Awareness Test: FXS Only

| **Rhyming<br>Raw** | **Raw Score<br>11.50 ( 4.42)** | **%ile (based on reading)<br>6.80 (10.36)** |
|---|---|---|
| Segmentation<br>Raw | 6.67 ( 5.35) | 8.33 ( 9.50) |
| Isolation (w/o *Medial*)<br>Raw | 8.67 ( 7.86) | 2.17 ( 3.49) |
| Deletion<br>Raw | 9.33 ( 6.68) | 7.83 (13.69) |