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Arousal Modulation in Females with Fragile X or Turner Syndrome

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Abstract The present study was carried out to examine physiological arousal modulation (heart activity and skin conductance, across baseline and cognitive tasks, in females with fragile X or Turner syndrome and a comparison group of females with neither syndrome. Relative to the comparison group, for whom a greater increase in skin conductance was associated with poor arithmetic performance and less risk taking behavior, females with fragile X displayed a minimal increase in heart activity that was nevertheless associated with poor performance on mental arithmetic. In contrast, no arousal–cognitive performance relationship emerged for the group with Turner syndrome. Taken together, our findings suggest that distinct profiles of arousal modulation might be associated with cognitive deficits in these syndrome populations.

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Arousal Modulation and Cognitive Task Performance in Females with Fragile X or Turner Syndrome

Between-syndrome comparative studies are a promising line of research that serve to differentiate shared from unique syndromic characteristics (Dykens, 2000). In particular, comparative studies with disorders having distinct cognitive profiles may refine phenotypes in ways that may ''fast track'' our understanding of gene function and promote our understanding of the relationship of genes, brain, and behavior (Dykens, 2000). Fragile X and Turner syndrome are two genetic disorders associated with cognitive and psychosocial difficulties. Phenotypic similarities across females with either disorder include social skills difficulties, heightened anxiety, weak arithmetic skills, and poor attention (as reviewed by Keysor & Mazzocco, 2002).

In an initial study, we reported distinct patterns of arousal for these two groups at rest and during stressful cognitive tasks using mean baseline levels of arousal (Keysor, Mazzocco, McLeod, & Hoehn-Saric, 2002). However, this initial study did not examine modulation of arousal or the relationship of arousal modulation to cognitive performance. Modulation of arousal reflects a person's ability to attend and respond appropriately to environmental challenges and, while related, is different from mean baseline arousal, which reflects a person's characteristic steady-state during specific conditions.

Examining the relationship between arousal modulation and cognitive task performance will inform our

understanding of cognitive impairment in these two syndromes. Thus, the present study provides a novel extension of the initial study by examining physiological arousal modulation across multiple baseline and cognitive tasks, and the relationship of arousal modulation to cognitive task performance. Of interest is whether arousal modulation varies across tasks believed to mark areas of primary cognitive deficits for females with either fragile X or Turner syndrome. The rationale for this research approach is expanded upon following a brief review of each disorder.

Fragile X and Turner Syndromes

Fragile X Syndrome

Fragile X syndrome is a single gene mutation that occurs in approximately 1/4000 males and 1/8000 females (Turner, Webb, Wake, & Robinson, 1996). Most males with fragile X (Bailey, Hatton, & Skinner, 1998) and approximately 50% of females with the disorder (Rousseau et al., 1994) have mental retardation. Females with the disorder who do not have mental retardation may have learning disabilities and behavioral features including shyness and social anxiety, eye contact avoidance, poor attention, and difficulty initiating and maintaining conversation (as reviewed by Hagerman, 2002). Increasing evidence suggests that ''hyperarousal,'' or an elevated state of physiological arousal, underlies many features of the fragile X behavioral phenotype (Cohen, 1995), including decreased eye contact and aberrant communication skills (Belser & Sudhalter, 1995), heightened sensory reactivity (Miller et al., 1999), withdrawn behavior (Hessl et al., 2002), and autistic behavior (Roberts, Boccia, Bailey, Hatton, & Skinner, 2001). Findings from these studies suggest that hyperarousal across tasks and poor arousal modulation between tasks may be a unique feature associated with this syndrome, a notion further explored in the present study.

Turner Syndrome

Turner syndrome results from the partial or complete absence of the second X chromosome in females. It occurs in approximately 1/2000 to 1/5000 live female births (Hook & Warburton, 1983). In addition to the reported cognitive phenotype (as reviewed by Mazzocco, 2006), females with Turner syndrome are at risk for having social-behavioral problems related to immaturity, impulsivity, and hyperactivity (McCauley, Feuillan, Kushner, & Ross, 2001). Very little research has been devoted to arousal in this population, and so the present study is of particular importance for addressing this topic.

Psychophysiological Studies

Although studies of physiological arousal in neurodevelopmental disorders are increasing, our initial study is the only published work focused on arousal in females with fragile X and the only published study to examine physiological arousal in females with Turner syndrome (Keysor et al., 2002). In that study, we compared females with fragile X to females with Turner syndrome, and to a comparison group of females that had neither syndrome. Findings suggested no group differences in self-reported anxiety and little evidence of elevated arousal in females with fragile X. Females with Turner syndrome demonstrated elevated arousal in mean skin conductance, skin conductance fluctuation, and heart activity during task performance phases compared to females with fragile X and females in the comparison group. In contrast, females with fragile X demonstrated a greater range of skin conductance. As such, this initial study highlighted important syndrome differences in the profile of arousal when arousal was assessed using mean baseline levels. However, modulation of arousal is another way to examine syndrome differences in response to challenge, and is the focus of the present study.

Physiological Arousal and Cognitive Performance

Of particular interest in considering physiological arousal in fragile X and Turner syndromes is the relationship between arousal and cognitive performance. Examination of the relationship between physiological arousal and cognitive task performance is based on the theory that baseline autonomic state and modulation of arousal are related to individual differences in the ability to perceive, process, and respond to cognitive challenge. In general, high or low baseline arousal and poor modulation of arousal in response to challenge is associated with poor cognitive and behavioral outcomes. Evidence exists that individuals with high baseline vagal tone (parasympathetic function of heart activity) who suppressed vagal tone during presentation of cognitive tasks, are more accurate during working memory tasks than individuals with lower baseline vagal tone (Hansen, Johnsen, & Thayer, 2003). Similarly, suppression of blood pressure during mental arithmetic is associated with improved performance (Reyes del Paso, Gonzalez, & Hernandez, 2004).

In our initial study (introduced previously), females with fragile X or Turner syndrome and females in the comparison group performed similarly on divided attention and risk taking cognitive tasks. However, the females with fragile X were less accurate than the comparison group, and similar to the Turner group, on the mental arithmetic cognitive task. Although no relationship was found between arousal during cognitive task completion and performance for females with fragile X, a relationship between heightened mean skin conductance and fewer attempted mental arithmetic problems was reported for females with Turner syndrome. The observed results for both syndrome groups contrasted with those of the comparison group. In the comparison group, longer IBI (lower heart rate) was related to increased accuracy and a greater number of correct responses for mental arithmetic and to fewer risk-escape responses on the risk taking task. Again, these results are suggestive of important syndrome differences in the contribution of arousal to cognitive performance.

The purpose of the present study is to use multiple measures of arousal to examine the relationship of arousal modulation and cognitive performance in females with fragile X or Turner syndrome compared to a typically developing comparison group absent for both disorders. Inclusion of multiple measures of arousal and cognitive performance is critical to examine converging evidence across physiological systems that are complex and differentially sensitive to stress and challenge. Specifically, we were interested in the group differences on physiological arousal modulation (as measured by heart rate activity, vagal tone, and skin conductance) and in the relationship of modulation of physiological arousal (via change scores on these measures) to task performance. Given that fragile X and Turner syndrome are both characterized by heightened anxiety and poor arithmetic processing, we proposed that performance on measures reflecting these deficit areas would be associated with similar patterns of arousal modulation. Such information contributes to our understanding of the underlying mechanisms associated with these problem behaviors in these two genetic syndromes.

Method

Participants

These data were collected in our previous work, as reported elsewhere in more detail (Keysor et al., 2002). To summarize, the three age-matched groups included females with the full mutation of fragile X ($n = 13$) or Turner syndrome ($n = 11$), and females with neither disorder who were in the comparison group ($n = 14$). Females with fragile X were 13 to 22 years (Mean = 16.50 ± 3.1). Females with Turner syndrome were 12 to 20 years (Mean = 16.70 ± 3.1), and females in the comparison group were 12–17 years (Mean = 14.96 ± 1.7). Enrollment in any of these three groups was limited to individuals who did not have another known genetic disorder associated with developmental delay (e.g., Down syndrome) and who did not have a diagnosis of mental retardation. Consistent with previous findings, females with fragile X had lower IQ scores (Mean FSIQ = 88.5) than females with Turner syndrome (Mean FSIQ = 96.5) and the comparison group (Mean FSIQ = 108.9) who were not different from each other.

Measures

Each of these measures is described in greater detail in the earlier report (Keysor et al., 2002) and summarized here.

Cognitive Tasks

Three computerized tasks were chosen to examine physiological changes as a result of engaging in stressful cognitive tasks. The tasks included Mental Arithmetic, Divided Attention, and Risk-Taking Tasks. Participants were engaged in each task for approximately 5 minutes. Unlike our initial study that included multiple measures of mental arithmetic and divided attention (e.g., percent accuracy, number attempted, and number correct), the current study only includes percent accuracy for these two cognitive tasks because these variables were believed to be the best representation of performance, and we wanted to reduce variables to minimize multiple comparisons within this small sample.

During the Mental Arithmetic Task, the participant was asked to mentally add three one-digit numbers presented on a computer screen, and then to press the center key on a keypad (‘‘2’’) when she had the sum. The keypad entry triggered a set of possible solutions to appear. The participant chose her response by pressing a key corresponding to her choice. Points were given for each correct response, but all points were lost if four consecutive errors were made. When points were lost, a message appeared on the computer screen, indicating the loss, and encouraging continued effort. After each answer, the remaining time was displayed, along with a tally of correct answers, and the point

value of the next correct answer. The percentage of problems solved correctly was used as the performance measure.

During the Divided Attention Task (McLeod, Hoehn-Saric, Labib, & Greenblatt, 1988), a sequence of numbers appeared in the center of a computer monitor screen. As one number disappeared from the screen, another number appeared in its place. The participant was to watch this sequence of numbers carefully, and to respond according to the following rules: When the number ''5'' appeared on the screen, the participant was to indicate (with a keypad press) whether the number presented immediately after the ''5'' was greater than five. Additionally, participants were instructed to press a key as soon as possible each time a ''0'' appeared in the sequence. The percentage of times the subject accurately detected whether numbers after ''5'' exceeded five was used as the performance measure in this study.

On the Risk-Taking Task (McLeod et al., 1988), participants were asked to accumulate as many points as possible during a computerized task. It was possible to lose or gain points depending on individual responses. A left-key response (''1'') accumulated points, and as points continued to accumulate a green bar that appeared on the computer monitor screen increased in length. A right key response (''3'') saved trial points to a cumulative task total and ended the given trial. With a probability of 0.05, any left-key response could trigger the appearance of a red bar, which was a signal that twice the number of points accumulated from that particular trial would be subtracted from the cumulative task total. As a measure of risk-taking behavior, the number of left key presses prior to a right key press served as the variable of interest in this task, with a higher score indicating a higher risk behavior (more key presses before stopping).

Physiological Arousal Measures

Our initial study included gastrocnemius electromyographic activity and multiple measures of heart activity and skin conductance (e.g., range, fluctuations). In this study, however, we report only physiological arousal measures of heart activity and skin conductance modulation to focus on arousal measures that reflect sympathetic and/or parasympathetic activity, to limit variables to minimize multiple comparisons with our small sample size, and to focus upon novel analyses related to arousal modulation. All physiological measures were sampled at a rate of 350 times per second. Collection, amplification, decoding and analyses were completed using a Coulborn Instruments Lablinc Interface System (Lehigh Valley, PA), a Modular Instruments Processing Center (Malvern, PA), a Zytek 386 Tower Computer (Zytek Engineering, Inc., Baltimore, MD), and Modular Instruments software.

Interbeat interval (IBI) is a measure of heart activity that represents the milliseconds between the peak R-waves. IBI reflects general arousal with input of both the sympathetic and parasympathetic branches of the autonomic nervous system. To obtain the IBI we placed disposable electrodes on the right and left chest and on the right and left abdomen and used the EKG lead that most accurately represented the T wave and the QRS complex onset. Vagal tone is a measure of heart activity that reflects parasympathetic activity associated with rest and restorative functions. To generate vagal tone, the amplitude of respiratory sinus arrhytmia was quantified by estimating successive 500-ms windows of sequential IBIs using computer programs consistent with Porges' methods (1985).

Skin conductance reflects eccrine sweat gland activity innervated by the sympathetic branch of the autonomic nervous system. Skin conductance was recorded by placing electrodes on the volar surfaces of the index and middle fingers of the nondominant hand using electrode paste prepared according to procedures recommended by Fowles and colleagues (1981). A constant voltage electrodermograph monitored the skin conductance.

The procedures to collect and edit the physiological arousal data are identical to those reported earlier (Keysor et al., 2002). To summarize, all testing started at approximately 9:00 A.M. Participants were seated in a reclining chair in a room that was kept in constant dim illumination. Following a 15-minute initial baseline rest period, participants performed the Mental Arithmetic Task, the Divided Attention Task, and then the Risk-Taking Task, always in that sequence. Each task lasted approximately five minutes and was preceded by a 15-minute baseline period. Physiological measures were recorded for the full duration of each cognitive task, but only during the last five minutes of each baseline period.

Results

Modulation of Physiological Arousal and Cognitive Performance

We examined group differences in arousal modulation by calculating a change score (cognitive task minus preceding baseline) for each group of partici-

pants, for all three cognitive tasks (Table 1). We used mean values only, per each of the main physiological variables of interest (IBI, vagal tone, and skin conductance). In view of the distribution of values for change scores, nonparametric statistics were used via Kruskal Wallis analyses, with Mann Whitney U tests used for post-hoc analyses as appropriate. Performance on the cognitive tasks was measured as accuracy on the math and divided attention tasks, and as the amount of risk-taking on the risk task. We examined the relationship of arousal modulation to task performance via Spearman rank correlations between change scores and task performance. In cases where tied rankings emerged, tied test statistic and p values are reported. Correlations were examined separately for each group, as the research question driving this set of analyses concerned whether the modulation-performance associations differed across groups.

IBI Change Score

For mean IBI values, there were no significant group differences for change scores between the cognitive tasks and preceding baseline measures, all *p* values > .22.

IBI Change Score and Performance

Different correlations emerged between IBI change score and performance, across the three cognitive tasks. For all three groups combined, there was a significant correlation between change score and performance on the mental arithmetic task, $r_s = .32$, $p = .05$. The correlation was statistically significant only in the fragile X group, $r_s = .59$, $p = .04$, all remaining *p*s > .20. In contrast, there was no significant correlation between change score and overall performance accuracy on the divided attention and risk taking tasks, either for the three groups combined, all *p*s > .80, or for the three groups individually, all *p*s > .20.

Vagal Tone Change Score

For mean vagal tone, there were no significant group differences for change scores between task and preceding baseline measures with all 3 groups included, all *p*s > .27.

Vagal Tone Change Score and Performance

There was no significant correlation between change score and performance accuracy on any of the three cognitive tasks, among either the entire group or any of the three participant groups, all *p*s > .18.

Skin Conductance Change Scores

There was a main effect of group on change in skin conductance between initial baseline and the mental arithmetic task, $H = 7.78$, $p = .02$. There was no main effect for change score with divided attention or risk taking tasks, all *ps* > .09. Post hoc comparisons for the mental arithmetic task revealed that females with fragile X displayed *smaller* change scores ($M = 1.05$) than the Turner syndrome group ($M = 4.01$), $U = -2.41$, $p = .02$, and the comparison group ($M = 2.12$), $U = -1.9$, $p = .05$. Mean change scores did not differ between the comparison group and the Turner syndrome group, $p = .13$.

Table 1 Mean (SD) of arousal change scores of preceding baseline to each cognitive task

Arousal index raw score	Fragile X syndrome	Turner syndrome	Comparison
Inter-beat-interval			
Mental arithmetic	–14.57 (64.0)	–40.1 (29.5)	–50.8 (60.3)
Divided attention	–27.4 (45.0)	–40.1 (30.9)	–18.5 (45.3)
Risk-taking	–23.8 (55.3)	–44.1 (45.1)	–37.5 (54.6)
Vagal tone			
Mental arithmetic	–.48 (1.2)	–.94 (1.1)	–.41 (.79)
Divided attention	–.64 (.75)	–.86 (.66)	–.35 (.71)
Risk-taking	–.51 (.79)	–.80 (1.0)	–59 (.74)
Skin conductance			
Mental arithmetic	1.05 (1.9)[a,b]	4.05 (2.88)	2.12 (1.56)
Divided attention	.65 (2.0)	3.50 (3.82)	2.01 (1.84)
Risk-taking	.71 (3.05)	1.6 (2.30)	2.67 (2.66)

[a] Significantly different from the Comparison group, $p = .05$

[b] Significantly different from the Turner syndrome group, $p < .05$

Skin Conductance Change Scores and Performance

The correlation between the change score and performance on the mental arithmetic task was significant for all groups combined, $r_s = -35$, $p = .03$. However, within groups, this correlation was significant only for the comparison group, $r_s = -.70$, $p = .01$, remaining group ps $> .11$. Correlations between the change and performance scores on the divided attention task were not significant overall or for any one group, all ps $> .15$. On the risk taking task, for all groups combined there was no significant association, $r_s = .28$, $p = .09$. Within groups, the correlation was significant only for the comparison group, $r_s = .57$, $p = .04$, remaining $ps > .38$.

Discussion

The purpose of the present study was to follow up on our initial study by examining physiological arousal modulation and its relationship to cognitive performance in females with fragile X or Turner syndrome, relative to age-matched females with neither syndrome. Such findings have not yet been reported in the literature on either syndrome. Our approach, comparing two genetic syndromes and a non-syndrome comparison group on multiple measures of arousal, is a promising line of research (Dykens, 2000) that may increase our understanding of shared and unique features of arousal abnormalities, cognitive task performance and the relationship between arousal and task performance in these two groups.

Modulation of physiological arousal revealed novel and potentially interesting group and task differences. In our previous work, we did not examine modulation over time. We reported that elevated mean arousal levels occurred only at baseline in females with fragile X syndrome, relative to the comparison group; whereas females with Turner syndrome had elevated mean arousal levels during completion of all cognitive tasks, relative to the comparison group; and during divided attention, relative to females with fragile X (Keysor et al., 2002). In the present study, we found no group differences in arousal modulation of heart activity (IBI and vagal tone) to any of the three cognitive tasks. Yet females with fragile X displayed smaller skin conductance change scores in comparison to the Turner syndrome and comparison groups for mental arithmetic but not for divided attention and risk-taking tasks. This suggests that females with fragile X display a flat modulation pattern of sympathetic activity in response to completing mental arithmetic, a cognitive task well characterized as difficult for females with fragile X. Interestingly, there was no relationship of arousal modulation and mental arithmetic in females with Turner syndrome, a group also characterized as having difficulty with mental arithmetic. In addition, the relationship of arousal modulation to mental arithmetic in fragile X was exclusive to skin conductance (an indicator of sympathetic activity) and not shown in IBI and vagal tone. Thus, our findings suggest that failure to increase sympathetic activity during specific cognitive challenges may be uniquely associated among females with fragile X, whereas other factors might be associated with poor arithmetic processing in females with Turner syndrome.

Results examining the relationship of arousal change scores to cognitive task performance suggested different relationships between groups across the various cognitive tasks. Our previous findings suggested a relationship between elevated arousal in Turner syndrome and fewer attempted mental arithmetic problems, decreased arousal to improved performance in mental arithmetic and increased arousal to more risk responses in the comparison group, and no arousal–performance relationships in the group with fragile X. In the present study, there was no relationship of any arousal change scores to performance on any of the three cognitive tasks in females with Turner syndrome. For females in the comparison group, increased modulation of skin conductance was associated with poorer performance on mental arithmetic and a higher rate of risk escape behavior (less willing to take risks). Given that sympathetic activity reflects the ''fight or flight'' response of the autonomic nervous system to respond to challenge, it seems that ''too much'' sympathetic activity is associated with poor cognitive performance in the comparison group, at least as measured by skin conductance.

Our finding that insufficient modulation of arousal is related only to poor performance on mental arithmetic and not to the other cognitive tasks in fragile X suggests that arousal modulation abnormalities (insufficient modulation) may be an underlying mechanism associated with deficits in mental arithmetic in women with fragile X. As noted, females with fragile X characteristically have poor arithmetic reasoning skills and, in fact, our sample of females with fragile X performed more poorly on our mental arithmetic task compared to the comparison group (82% and 93% accuracy respectively). However, they performed similarly to the females with Turner syndrome (83% accuracy) despite lower IQ in the group with fragile X. Thus, within the group of females with fragile X there may be individual differences in arousal modulation that par-

tially explain performance in arithmetic computation. Limited support for this hypothesis comes from the lack of an observed relationship between IBI suppression, divided attention and risk-taking in the fragile X group. This finding suggests that arousal modulation may be more critical for success on tasks that are characteristically more difficult for females with fragile X, such as mental arithmetic. This is consistent with recent functional MRI studies that reported less differential brain activation in response to increased cognitive difficulty among females with fragile X (Kwon et al., 2001; Tamm, Menon, Johnston, Hessl, & Reiss, 2002).

Differences between our initial and current findings highlight the importance of investigating arousal during specific conditions in addition to examining arousal modulation in response to environmental challenges. Specifically, our initial study reported tentative support that females with fragile X display hyperarousal that was not related to cognitive performance. However, the current study suggests that females with fragile X may have problems with inadequate arousal modulation that is related to their poor performance on mental arithmetic. With regard to females with Turner syndrome, our initial study reported elevated arousal during all cognitive tasks and a relationship with elevated arousal to fewer attempted mental arithmetic problems. The current study, however, suggests no differences in arousal modulation in females with Turner syndrome compared to fragile X or a comparison group and no relationship of arousal modulation to cognitive performance.

In view of the existing literature and our studies, some interesting arousal–cognitive performance profiles are suggested. Females with fragile X exhibit a profile of moderate levels of arousal but insufficient modulation of arousal that is associated with poor cognitive performance (Kwon et al., 2001; Tamm et al., 2002). Females with Turner syndrome display a profile of elevated mean levels of arousal associated with cognitive difficulties, yet, no association between arousal modulation is supported (Keysor et al., 2002 ; Skuse, Morris, & Dolan, 2005). Typically developing females display a profile of moderate levels of arousal and insufficient or excessive modulation of arousal associated with poor cognitive performance (Althaus, Mulder, Mulder, Aarnoudse, & Minderaa, 1999; Rypman, Berger, Genova, Rebbechi, & D'Esposito, 2005). However, given the limited investigation of arousal in females with fragile X or Turner syndrome and the descriptive nature of our work, these profiles are speculative until confirmed by larger, more systematic studies.

Although findings from our current study contribute important information about females with fragile X or Turner syndrome, there are limitations to this study. Most notably, our small sample size limits our power to detect group differences and correct for multiple comparisons. In addition, the small sample size, lack of genetic (e.g., FMRP in fragile X group) and hormonal (e.g., estrogen in Turner group) data, and wide age range precluded our ability to examine these potentially important within group factors. Despite these limitations, this study provides important preliminary evidence of arousal differences in these two genetic syndromes.

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References

Althaus, M., Mulder, L. J., Mulder, G., Aarnoudse, C. C., & Minderaa, R. B. (1999). Cardiac adaptivity to attention-demanding tasks in children with a pervasive developmental disorder not otherwise specified (PDD-NOS). *Biological Psychiatry, 46*, 799–809.

Bailey, D. B. Jr., Hatton, D. D., & Skinner, M. (1998). Early developmental trajectories of males with fragile X syndrome. *American Journal on Mental Retardation, 1*, 29–39.

Belser, R. C., & Sudhalter, V. (1995). Arousal difficulties in males with fragile X syndrome: A preliminary report. *Developmental Brain Dysfunction, 8*, 270–279.

Cohen, I. L. (1995). Behavioral profiles of autistic and nonautistic fragile X males. *Developmental Brain Dysfunction, 8*, 252–269.

Dykens, E. M. (2000). Psychopathology in children with intellectual disability. *Journal of Child Psychology & Psychiatry, 41*, 407–417.

Fowles, D. C., Christie, M. J., Edelberg, R., Grings, W. W., Lykken, D. T., & Venables, P. H. (1981). Publication recommendations for electrodermal measurements. *Psychophysiology, 18*, 232–239.

Hagerman, R. J. (2002). The physical and behavioral phenotype. In R. J. Hagerman & P. J. Hagerman (Eds.) *Fragile X syndrome: Diagnosis, treatment, and research* (3rd ed., pp. 206–248). Baltimore: Johns Hopkins University Press.

Hansen, A. L., Johnsen, B. H., & Thayer, J. F. (2003). Vagal influence on working memory and attention. *International Journal of Psychophysiology, 48*, 263–74.

Hessl, D., Glaser, B., Dyer-Friedman, J., Blasey, C., Hastie, T., Gunnar, M., et al. (2002). Cortisol and behavior in fragile X syndrome. *Psychoneuroendocinology, 27*, 855–72.

Hook, E. B., & Warburton, D. (1983). The distribution of chromosomal genotypes associated with Turner's syndrome: Livebirth prevalence rates and evidence for diminished fetal

mortality and severity in genotypes associated with structural X abnormalities or mosaicism. *Human Genetics, 64*, 24–27.

Keysor, C. S., & Mazzocco, M. M. M. (2002). A developmental approach to understanding fragile X syndrome in females. *Microscopy Research and Technique, 57*, 179–186.

Keysor, C. S., Mazzocco, M. M., McLeod, D. R., & Hoehn-Saric, R. (2002). Physiological arousal in females with fragile X or Turner syndrome. *Developmental Psychobiology, 41*, 133–146.

Kwon, H., Menon, V., Eliez, S., Warsofsky, I. S., White, C. D., Dyer-Friedman, J., et al. (2001). Functional neuroanatomy of visuospatial working memory in fragile X syndrome: relation to behavioral and molecular measures. *American Journal of Psychiatry, 158*, 1040–1051.

Mazzocco, M. M. M. (2006). The cognitive phenotype of Turner syndrome: Specific learning disabilities. *International Congress Series, 1298*, 83–92.

McCauley, E., Feuillan, P., Kushner, H., & Ross, J. L. (2001). Psychosocial development in adolescents with Turner syndrome. *Journal of Behavioral and Developmental Pediatrics, 22*, 360–365.

McLeod, D. R., Hoehn-Saric, R., Labib, A. S., & Greenblatt, D. J. (1988). Six weeks of diazepam treatment in normal women: Effects on psychomotor performance and psychophysiology. *Journal of Clinical Psychopharmacology, 8*, 83–99.

Miller, L. J., McIntosh, D. N., McGrath, J., Shyu, V., Lampe, M., Taylor, A. K., et al. (1999). Electrodermal responses to sensory stimuli in individuals with fragile X syndrome: a preliminary report. *American Journal of Medical Genetics, 4*, 268–279.

Porges, S. W. (1985, April). Method and apparatus for evaluating rhythmic oscillations in aperiodic physiological response systems. U. S. Patent 451 0944.

Reyes Del Paso, G. A., Gonzalez, E., & Hernandez, J. A. (2004). Baroreceptor sensitivity and effectiveness varies differentially as a function of cognitive-attentional demands. *Biological Psychology, 67*, 385–395.

Roberts, J. E., Boccia, M. L., Bailey, D. B., Hatton, D. H., & Skinner, M. (2001). Cardiovascular indices of psychophysiological arousal in boys with fragile X syndrome. *Developmental Psychobiology, 39*, 107–123.

Rousseau, F., Heitz, D., Tarleton, J., MacPherson, J., Malmgren, H., Dahl, N., et al. (1994). A multicenter study on genotype-phenotype correlations in the fragile X syndrome, using direct diagnosis with probe StB12.3: the first 2,253 cases. *American Journal of Human Genetics, 55*, 225–237.

Rypman, B., Berger, J. S., Genova, H. M., Rebbechi, D., & D'Esposito, M. (2005). Dissociating age-related changed in cognitive strategy and neural efficiency using event-related fMRI. *Cortex, 41*, 582–594.

Skuse, D. H., Morris, J. S., & Dolan, R. J. (2005). Functional dissociation of amygdala-modulated arousal and cognitive appraisal, in Turner syndrome. *Brain, 128*, 2084–2096.

Tamm, L., Menon, V., Johnston, C. K., Hessl, D. R., & Reiss, A. L. (2002). fMRI study of cognitive interference processing in females with fragile X syndrome. *Journal of Cognitive Neuroscience, 14*, 160–171.

Turner, G., Webb, T., Wake, S., & Robinson, H. (1996). Prevalence of the fragile X syndrome. *American Journal of Medical Genetics, 64*, 196–197.