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Facial Affect as a Component of Emotion Regulation During Inhibitory Control in FXS

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FACIAL AFFECT AS A COMPONENT OF EMOTION REGULATION DURING INHIBITORY CONTROL IN FXS

By

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Abstract

The present study investigated emotion regulation through facial affect during inhibitory control in FXS. Male participants (N=32) were asked to complete a task that induced frustration. An M&M was placed in front of the subject, and they were instructed not to eat the M&M until the trial has ended, marked by the ringing of a bell. The subject's facial affect was observed and recorded throughout the 6 trials to investigate the differences between the emotion regulation of TD and FXS children. It was hypothesized that the TD group would be less expressive, and more negative than the TD children. It was found that the children with FXS remained more neutral throughout the trials, compared to the TD group. These results are potentially indicative of differences in emotion regulation in children with FXS.

Keywords: Fragile X syndrome, emotion regulation, inhibitory control

Introduction

Facial affect as a component of emotion regulation during inhibitory control in FXS

Fragile X Syndrome (FXS) is an x-linked genetic disorder that arises due to a mutation on the *FMR1* gene that leads to varying levels of intellectual disability. FXS occurs in both males and females; however, males often experience more impairing symptoms, perhaps due to X chromosome inactivation in females (Crawford et al., 2001). Categorized as an inherited intellectual and developmental disability (IID), FXS impacts multiple areas of functioning, including learning, social, behavioral, emotional, speech, and language abilities (US Department of Health and Human Services, n.d.). Additionally, there is a high rate of psychiatric comorbidities in individuals with FXS, such as anxiety, ADHD, and autism spectrum disorder (ASD), that introduce additional developmental difficulties (McKechanie et al., 2019).

At present, no known medications have been developed that are specifically designed for individuals with FXS, however existing medications such as selective serotonin reuptake inhibitors and stimulants have proven successful in reducing behavioral and emotional symptoms in FXS. Research on other neurodevelopmental disorders, such as ASD, has highlighted the effectiveness of early intervention targeting emotional, behavioral, intellectual, and adaptive functioning impairments (Hall, 2009). These early intervention strategies have shown a more positive outlook in the treatment of the symptoms associated with FXS (Hall, 2009), and thus may be effective strategies to co-opt and adapt for the treatment of FXS. If left untreated, early behavioral, and emotional problems may increase with age or lead to more severe psychiatric outcomes (Black et al., 2021). Thus, early intervention is necessary to ensure the best care and outlook for individuals with FXS.

Because early intervention is associated with more optimal outcomes in children with neurodevelopmental disorders, early identification of FXS is critical. Research examining the early behavioral phenotype of FXS may also improve early detection, especially for families with no known history of *FMR1*-related conditions or who forgo prenatal genetic testing. One recent study determined physiological and behavioral manifestations of social anxiety are evident as early as 12 months in children with FXS, which could potentially be utilized as early identification markers (Black et al., 2021). While some of the hallmark behavioral symptoms may not become noticeable until later in childhood, there are several medical conditions associated with FXS, such as low birth weight, otitis media, seizures, mitral valve prolapse, sleep and GI problems, that may present at an earlier age (Lozano et al., 2016). These conditions, while not necessarily indicative of FXS, could be help identify some FXS cases during infancy and early childhood.

Emotion Regulation/IC/EF in Typical Development

Emotion regulation is the ability to utilize effective strategies to manage one's own range of emotions. These abilities begin to develop in infancy and becomes more sophisticated as children age. The ability to regulate emotional arousal and react to stimuli is built from situations conducive to practicing that regulation. In toddlerhood, typically developing children begin to differentiate between happy and sad emotions, emote aggressively, control their behavior, and build the capacity to delay gratification, which is a form of inhibitory control (Crowell, 2021). There is also a sensitive period between the ages of three and six, in which typically developing children exhibit rapid growth in the capacity to control their emotions and cope with distress; this may be explained in part by concurrent improvements in effortful control and executive function, both of which are important in the overall capacity for emotion regulation and are underpinned

by inhibitory control (Bridgett et al., 2013). The present study included children within this age range in order to capture this pivotal period of emotion regulation development.

IC/ER/EF deficits in FXS

Though little to no research has examined the behavioral presentation or underlying processes of emotion regulation in FXS, the early temperamental and executive profiles of children with FXS have been well characterized. A study by Low Kapalu and Garstein (2016), found that children with FXS exhibit less facial reactivity, extraversion, and effortful control, which culminate in differences in temperament. This study additionally concluded that in FXS, there appeared to be a higher level of activity, shyness, attention deficits, inhibitory control, and less intense emotional response to positive stimuli. In addition to observed differences in temperament, FXS has been associated with executive functioning deficits. These deficits seen in children with FXS, are more extreme than what is typically seen for various developmental delays and are increased due to the neurocognitive deficits seen in many FXS cases (Hooper, et al, 2008).

Facial affect as a marker of ER in TD

Greater effortful control has been associated with greater ability to regulate negative facial expressions in children ages 51-72 months (Carlson et al., 2007). Indeed, the ability to control facial expression increases with age (Cole, 1986). At a young age, children gain control of the muscular movements underlying various facial expressions, and as they age, they typically have greater control over time (Nelson, 1987). This development generally leads to an overall decrease in facial expressiveness overtime. In TD children, it is common to see them attempt to control their negative emotion by masking it with positive displays (Dennis et al., 2009). Effective regulation of facial expression requires both awareness of what behaviors and emotions

are socially acceptable and execution of inhibitory control to adjust their behavior in accordance with this knowledge (Hudson & Jacques, 2014). A study investigating facial expressiveness during pain and disgust found that children with greater inhibitory control displayed less negative facial affect, indicate a connection between inhibitory mechanisms and the downregulation of facial expressiveness (Karmann, et al., 2015). Together, these findings suggest greater expression of negative facial affect may be an indicator of impaired or delayed executive function development in children.

Facial affect in FXS

Studies of early temperament and facial expressivity have found that children with FXS generally express less positive facial affect, specifically smiling and laughter, during infancy compared to TD infants (Tonnsen, et al., 2018). Additionally, a study of temperament and social adjustment found that the male subjects with FXS were slower to adapt, more cautious, more serious, and less persistent compared to the TD subjects (Ury, 1999). Overall, these studies suggest that children with FXS have less emotional reactivity, and when they are expressive, it is generally more negative, compared to TD children (Wall et al., 2019). However, it has not been determined whether blunted or greater negative affect is associated with inhibitory control impairments in FXS. Given that valid assessment of inhibitory control performance in children with FXS proves difficult due to the presence of intellectual disability, facial affect may serve as an alternative and sensitive indicator of regulatory deficits. These markers may inform the behavioral phenotype of children with FXS as well as potential treatment targets for this group. More broadly, a better understanding of emotion regulation challenges in FXS is necessary to adapt developmental expectations and environmental fit for these children.

Objective

Given inhibitory control is an essential underpinning of emotion regulation and successful emotion regulation is demonstrated through modulated facial affect, the present study will investigate the association between inhibitory control and facial affect in children with FXS. It is hypothesized that children with FXS will exhibit greater difficulty controlling their facial expressions during a challenging delay task, and therefore will be overall more expressive than the TD children. It also is expected that FXS children will display more negative emotions such as anger, frustration, and sadness, than the TD children, who are expected to exhibit more positive facial affect, such as smiling and laughing. Findings may provide insight into the development of emotion regulation in children with FXS and whether this differs from typical development. As previously discussed, earlier intervention can help in reducing emotional and behavioral symptom impairment in FXS. These findings could be beneficial in identifying early markers and targets for intervention in children with FXS.

Method

Participants

The present sample was from ongoing longitudinal studies examining the development of children with FXS at the University of South Carolina (R01MH107573, R01MH090194; PI: Roberts). Participants included children with FXS or typically developing children who completed an assessment between the ages of 3-5 years. Diagnosis of FXS was confirmed through genetic report. Typically developing children with a family history of ASD, FXS, or related disorders or who were born preterm were excluded. The resulting sample included 32 male subjects, 16 children with FXS (*M*=48.6, *SD*=7.38), and 16 typically developing children (*M*=47.9, 6.96). Groups were matched on chronological age.

Measures

Developmental Ability. The Mullen Scales of Early Learning (*MSEL;* Mullen, 1995) was administered to assess the cognitive development of the subjects. This standardized test, generally used for children aged 0-68 months, assesses fine motor, visual reception, receptive language, and expressive language skills. The MSEL- Early Learning Composite Score was used as a measure of developmental ability.

Inhibitory Control. ***Parent rating.*** The Children's Behavior Questionnaire (*CBQ;* Rothbart, et al., 2001) was used as a parent-report measure of child temperament. This survey evaluates different facets of child behavior, including inhibitory control, smiling and laughter, fear, anger/frustration, and discomfort, via parent-rating on a Likert scale. Parents rate the frequency of these behaviors and emotions as seen in the child's typical, daily activities. This study utilized inhibitory control, negative affect (discomfort, anger, frustration), and positive affect (smiling and laughing) subscales from the CBQ.

Observational Measure. The Snack Delay episode from the Laboratory Temperament Assessment Battery – Preschool Version (Lab-TAB; (Goldsmith & Rothbart, 1996) was used. Chi-squared analyses were run to evaluate group differences in performance on the Snack Delay task. The variables were coded (0/1) as failure/pass of the trial, waiting or failing to wait. We computed an overall performance variable which indicates passing on all trials (1), vs failing on any trial (0).

During the Snack Delay Task, an M&M is placed under a clear container in front of the child, and the child is instructed to not eat the M&M until the examiner rings a bell. The tasks consist of six trials of varying lengths, though only the four trials with delay lengths greater than 0 seconds were analyzed (i.e., 5-, 10-, 20-, and 30-second trials). Performance on each trial was

rated as pass/fail, indicating the child waited the full duration of the trial or ate the M&M prematurely. Facial expression of the child during the delay period was also observed as an index of emotional regulation capacity. Adapted from the Facial Action Coding System (FACS; Ekman & Friesen, 1978), an anatomically based facial affect coding system based on observable muscle movements, and coding systems developed by Jahromi et al. (2012), two metrics of facial expressiveness were analyzed in the present study: overall facial affect and eye constriction behavior. Video recordings of the Snack Delay task were analyzed using Datavyu observational coding software. Facial affect was categorized as positive, neutral, or negative. Eye constriction was categorized as constricted, neutral, or widened. Both dimensions were coded continuously across each trial, and proportions of each category of facial affect and eye constriction during each trial were calculated. The number of facial affect changes across the trial was also noted. Through preparation and refinement of coding methods, inter-rater reliability (80%) was established between two independent coders and maintained on 20% of video files.

Procedure

Procedures were approved by the Institutional Review Board at the University of South Carolina. Parents of children offered informed consent to be enrolled in the study. Assessments were completed in a research laboratory setting or the child's home. Families were compensated for their participation.

Statistical Analysis Plan

To examine group differences in proportions of facial affect categories, independent samples *t*-tests were run. T-tests were also used to determine the correlation of different aspects of parent-reported temperament. Chi-squared analyses were used to assess group differences (TD, FXS) on trial performance of the M&M task on each trial and overall success or failure.

Results

Descriptive statistics of developmental ability and temperament domains by group are presented in Table 1. Correlational analyses examining the association between IC and SL and IC and NA were examined for each group. In the TD group, there was a positive correlation (r=0.49, p=.060) between IC and SL. For the FXS group, there was a moderate positive association between IC and SL (r=.60, p=.023). There was a negative association between IC and NA for both the TD group, (r=-0.54, p=.039). There was no association found between IC and NA in the FXS group (r=-0.18, p=.540). Together, these results suggest that greater inhibitory control is associated with greater positive facial affect and less negative affect in both groups regardless of whether the child is TD or has FXS.

Group differences were evaluated for performance on the Snack Delay task. Groups significantly differed on understanding of the task, (X^2(1, N=32) =13.33, p=0.0003, OR=0.03 [95% CI= 0.0031,0.29]), such that TD children were 33 times more likely to understand the rules and expectations. The TD group was also significantly more likely than the FXS group to pass the 5-second trial, (X^2(1, N=32)=7.58, p=0.006,), 10-second trial, (X^2(1, N=31)= 9.57, p=0.002), 20-second trial, (X^2(1, N=32)=10.49, p=0.0012,), and 30-second trial, (X^2(1, N=31)= 5.43, p=0.020,). These results suggest that the TD group was more likely to pass the task at all levels of difficulty. A chi-squared analysis for those who passed all of the trials versus those who failed one or more trials not in the FXS and TD groups was also statistically significant (X^2(1, N=32)= 6.15, p=0.013, OR=0.15 [95% CI= 0.032,0.71]), indicating TD children were 6.6 times more likely than the FXS children to pass every trial.

For the 30-second trial of the Snack Delay task, the proportion of time spent exhibiting each valence of facial expression (positive, negative, neutral) was calculated and averaged for

both groups (Table 3). Independent samples t-tests were run to determine group differences in proportions for each facial expression valence category. Groups significantly differed on expression of positive affect ($t(30)= -2.71$, $p=.012$) and neutral affect ($t(30)=2.24$, $p=.034$), such that FXS children expressed significantly less positive and more neutral affect than TD children during the 30-second trial of the Snack Delay task. There was no group difference in expression of negative affect ($t(30)=1.45$, $p=.167$).

Eye constriction was coded and analyzed in the same manner as the overall facial affect during the 30-second trial of the Snack Delay task. The proportions, in seconds, of each eye constriction position are presented in Table 4. Independent samples t-tests were run to determine group differences in eye constriction. Groups significantly differed in proportion of trial with neutral eyes ($t(30)=2.24$, $p=.034$) and marginally significantly differed in proportion of trial with constricted eyes ($t(30)=-2.05$, $p=.053$), such that FXS children used significantly less eye constriction and more neutral eyes than TD children during the 30-second trial of the Snack Delay task. There was no group difference in eye-widening ($t(30)=0.70$, $p=.493$).

Discussion

The present study evaluated differences in emotion regulation between children with FXS and TD children via facial affect, eye constriction, and performance on a delay of gratification test (i.e., Snack Delay task), and parent-reported temperament measures.

The main objective of this project was to characterize behavioral manifestations of inhibitory control in childhood in children with FXS compared to TD children. Our findings corroborate previous research demonstrating inhibitory control deficits in children with FXS (Low Kapalu & Gartstein, 2016). In all 4 experimental trials of the Snack Delay task, the pass rate was significantly higher for the TD group than the FXS group (Table 2), suggesting children

with FXS in this age range experience greater difficulties with inhibitory control during delay than age-matched typical peers. IC deficits in children with FXS can have a wide range of effects academically, emotionally, and socially. IC deficits are related to impaired response inhibition (Schmitt, et al., 2017), which could manifest in less self-control in social interactions and less ability to control emotional responses and reaction formation. IC deficits are shown to be associated with aggression and attention problems in preschool age children (Raajjmakers, 2008), which could negatively impact social relationships and ability to focus in classrooms, potentially causing disruptions or having trouble learning in a typical classroom setting.

Our results indicate children with FXS tend to display less positive and more neutral facial affect compared to their TD counterparts during the delay task, which may be indicative of a difference in emotion regulation between the two groups. Interestingly, both groups exhibited minimal negative affect throughout the trial. This could be a result of the task being too easy for the TD group to elicit a frustrated response and, and the FXS group not fully understanding the task, and eating the M&M too quickly for the task to elicit a frustrating response in either group. These results are surprising given that other studies have indicated that male, toddler-age children with FXS exhibit greater negative affect compared to their TD counterparts in relation to anxiety (Wall, et al., 2019). Greater inhibitory control is associated with a downregulation of facial expressiveness in pain and disgust (Karmann, et al, 2015), which would lead one to think that in those with IC deficits, there would be more negative expressivity. The results differ from the hypothesis that the FXS children would display more negative facial affect. This could be due to the FXS children not becoming frustrated from the task because they did not wait for the bell to eat the M&M. These findings are not consistent with the finding that the FXS children would display more negative affect but are consistent with several studies suggesting that FXS

children often remain more neutral (Wall, et al., 2019; Shanahan et al., 2008). It is possible that TD children may use smiling as a coping mechanism during frustration more frequently than FXS children, who were shown to stay more neutral during the task (Jahromi, et al, 2012).

Eye constriction is an aspect of facial affect, as the eyes have been shown to be the most expressive part of the face (Qiao, 1989), which is why it was analyzed as a separate component. It was found that the TD group had a greater amount of eye constriction compared to the FXS group, whereas the FXS group exhibited greater neutral eye shape. Given the FXS group expressed more neutral facial affect, it is expected that their eye constriction would also be more neutral, which was supported by the data. In addition, it was seen that the TD group expressed more positive facial affect overall, in addition to more eye constriction, which is typically seen with smiling and laughter. Low eye constriction of the FXS suggests greater neutrality of facial expressions compared to the TD group.

In addition to examining differences in performance and behavior in vivo during a task of inhibitory control, more global parent-ratings of child temperament were assessed. Parent ratings of child inhibitory control and smiling and laughter were positively related in the TD group, suggesting greater inhibitory control is associated with greater displays of smiling and laughter. Additionally, a negative correlation was found for inhibitory control and negative affect in the TD group, indicating TD children with greater the inhibitory control express less negative affect. These findings together indicate that TD subjects with more inhibitory control display more positive expressions and less negative expressions. Additionally, there was a significant positive association found between inhibitory control and smiling and laughter in the FXS group. This could be due to the FXS group having less inhibitory control and displaying less positive affect. There was no association found between inhibitory control and negative facial affect. The

associations found between IC and SL for both groups are consistent with previous studies. Greater IC would allow a child to better regulate their emotions and therefore it would be expected that those with higher IC would display less negative affect. Though these findings are consistent with our hypothesis of differences in emotion regulation between groups, additional questions are introduced. These results could indicate that inhibitory control development is slowed in FXS and therefore the expected association between negative affect and inhibitory control is not evident at low levels of inhibitory control. It is also possible that FXS children emote differently than TD children independent of IC development. These findings suggest that FXS and TD children exhibit differences in inhibitory control and expression of facial affect, which may be indicative of differences in how they regulate their emotion. Further investigation of processes underlying emotion regulation is necessary to understand developmental differences of children with FXS.

Limitations

Limitations of this study include the timing of the trial and use of facial affect measure as a proxy for emotion regulation. First, the children's facial affect was analyzed for the last trial, which was beneficial because it was the longest of the trials (i.e., 30 seconds), but it also could have influenced the subject's attentiveness, due to fatigue or boredom from the task. Additionally, the majority of children with FXS did not wait the entire trial before eating the snack; thus, it is unclear whether their facial expressions across the full trial are reflective of emotion regulation, given there are no demands placed on them once they have eaten the snack.

Future directions

Future directions should include longitudinal assessment of emotion regulation via facial affect, which could provide more insight into the development and changes in the overt

manifestation of inhibitory control in FXS children compared to TD children. Additionally, it is important to identify tasks of inhibitory control and emotion regulation which children with FXS can perform with greater success in order to better understand these processes. The present study reported differences in developmental ability between groups. Future work should examine the role of developmental ability in inhibitory control, emotion regulation, or coping strategies and whether this drives group differences.

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Table 1

Descriptive Statistics by Group.

	FXS (*n*=16)	TD (*n*=16)
MSEL ELC, *M(SD)*	53.38 (6.70)	98.00 (18.64)
Inhibitory Control, *M(SD)*	3.16(0.91)	4.39(0.86)
Negative Affect, *M(SD)*	3.51(0.54)	3.64(0.74)
Smiling & Laughter, *M(SD)*	5.91(0.60)	6.19(0.60)

Note. Inhibitory control refers to the parent-reported ability of their child to override natural impulses for more goal-oriented or productive causes. The parents reported the negative affect, or negative expressions, that their children exhibit during their routine activities. The parents reported the smiling and laughter, their positive expressions, during routine tasks.

Table 2

Chi-squared analyses for Snack Delay Performance between TD and FXS

Variable	Group			
	FXS (n = 16)	TD (n = 16)	*p*-value	Test statistic
Impression of Understanding Task (n, %)	5 (31.3%)	15 (21.7%)	p =0.0003	X^2 = 13.333
Pass 5-second Trial, (n, %)	5 (31.3%)	15 (93.8%)	p =0.006	X^2 =7.575
Pass 10-second Trial, (n, %)	5 (33.3%)	14 (87.5%)	*p=0.002*	*X^2=9.574*
Pass 20-second Trial, (n, %)	5 (31.3%)	14 (87.5%)	*p=0.0012*	*X^2=10.494*
Pass 30-second Trial, (n, %)	5 (33.3%)	12(75%)	*p=0.020*	*X^2=5.427*
Passed All Trials, (n, %)	5 (31.3%)	12(75%)	*P=0.013*	*X^2=6.149*

Table 3

Independent t-test for facial affect of TD and FXS

	FXS (*n*=16)	TD (*n*=16)	*t*	*p*
Positive Affect, *M(SD)*	0.20 (0.25)	0.49 (0.36)	-2.71	0.012
Neutral Affect, *M(SD)*	0.74 (0.25)	0.50 (0.36)	2.24	0.034
Negative Affect, *M(SD)*	0.06 (0.14)	0.01 (0.02)	1.45	0.167

Table 4

Independent t-test for eye constriction of TD and FXS

	FXS (*n*=16)	TD (*n*=16)	*t*	*p*
Constricted, *M(SD)*	0.07 (0.13)	0.22 (0.26)	-2.05	0.053
Neutral, *M(SD)*	0.90 (0.16)	0.77 (0.25)	2.24	0.034
Widened, *M(SD)*	0.03 (0.11)	0.01 (0.04)	0.70	0.49