The Topographies and Operant Functions of Challenging Behaviours in Fragile X Syndrome: A Systematic Review and Analysis of Existing Data

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LITERATURE REVIEW

The topographies and operant functions of challenging behaviours in fragile X syndrome: A systematic review and analysis of existing data

Rebecca Lyndsey Hardiman and Peter McGill

Tizard Centre, University of Kent, Canterbury, UK

CONTACT Rebecca Lyndsey Hardiman rh432@kent.ac.uk

Abstract

Background Challenging behaviour, such as self-injury and physical aggression, is an issue of concern regarding a high proportion of individuals with fragile X syndrome. The aim of this review was to provide a comprehensive overview of the topographies and operant functions of challenging behaviours within the syndrome.

Method Five electronic databases were searched, identifying 18 manuscripts. Overall proportions of individuals with particular topographies of behaviour, or behaviour serving different functions, were calculated.

Results Across all participants, biting was the most common form of self-injury for males but not females. A pattern of behavioural function was observed, characterised by high levels of social-negative reinforcement, such as escape from demands.

Conclusion The existence of within-syndrome biases in the manifestation of behavioural challenges is supported by our review.

Introduction

Fragile X syndrome (FXS) is the leading known inherited cause of intellectual disability (ID), affecting approximately 1 in 4,000 males and 1 in 8,000 females (Mazzocco, 2000). The behavioural phenotype of the syndrome includes hyperactivity in addition to social anxiety, and typically presents more severely in males (Bailey, Raspa, Olmsted, & Holiday, 2008; Cordeiro, Ballinger, Hagerman, & Hessl, 2011). Carers report that behavioural issues are of the highest concern when supporting individuals with FXS (Hagerman, 2002). Of note, FXS has been associated with an increased risk for engaging in challenging behaviour, particularly self-injurious behaviour (SIB; Arron, Oliver, Berg, Moss, & Burbidge, 2011). In particular, hand biting is sometimes described as part of the behavioural phenotype (Hagerman, Amiri, & Cronister, 1991). In fact, a recent systematic review found that, across studies, 45% of males with FXS were reported to engage in SIB and 39% were reported to display aggressive behaviour. Consistent with the broader gender differences in presentation, significantly fewer females were reported to engage in challenging behaviour (Hardiman & McGill, 2014). Given the high prevalence and concern about these behaviours in FXS, there is a clear need to better understand their causes to better intervene and prevent their occurrence.

There has been a significant amount of research investigating general causes of and risk factors for challenging behaviour. One prominent explanatory model is based upon the principles of operant reinforcement. According to this approach, which is supported by a wealth of evidence, challenging behaviours are learned through a process of reinforcement by their social or automatic consequences (Beavers, Iwata, & Lerman, 2013). Researchers in this have tended to focus largely upon the influence of the individual's external environment, such as the inadvertent reinforcement of challenging behaviour through provision of attention or tangible items, or removal of demands, following engagement in the behaviour (for a review, see Beavers et al., 2013).

However, a growing body of evidence supports that the risk for development of challenging behaviour varies with the genetic aetiology of ID. These findings suggest that there are syndrome-specific influences on challenging behaviours. This is problematic for the operant model, which cannot easily account for this uneven pattern of prevalence, due to the presumed random distribution of environments that provide necessary reinforcement for challenging behaviours (Arron et al., 2011). As such, recent theories have aimed to take a more holistic approach to understanding challenging behaviours, by incorporating these additional genetic influences into the established operant learning approach. For instance, Langthorne, McGill, and O'Reilly (2007) hypothesised that genetic syndromes may be associated with enduring motivational changes, which influence the operant learning of challenging behaviours. According to this approach, the reinforcing value of common responses to challenging behaviour may be unusually heightened or reduced in particular conditions. Heightened motivations may have an evocative effect upon behaviour, whereby behaviours that have been associated with the preferred reinforcer (including challenging behaviours) would occur more frequently. Therefore, even in constant environments, behavioural variability would be expected as a result of these genetically associated changes. If these motivational changes do exist, then one would expect there to be a bias towards a particular behavioural function within individuals with FXS. This assertion will be investigated in this review.

Furthermore, it is possible that alterations in the reinforcing properties of automatic or social consequences for behaviour may also influence the likelihood of developing particular topographies of challenging behaviour. Therefore, examination of patterns of behavioural topography within conditions may support the identification of specific risk factors for developing behavioural challenges. For example, skin picking is believed to be a characteristic topography of SIB in Prader–Willi syndrome. New findings suggest that this behaviour has specific physiological underpinnings, which are associated with automatically produced sensory reinforcement (Hustyi, Hammond, Rezvani, & Hall, 2013). This finding is prompting researchers to investigate biological correlates of this specific topography behaviour, which may have future implications for treatment (Hall, Hammond, & Hustyi, 2013; Hammond, Hall, Hustyi, & Reiss, 2013). In addition, people with Angelman syndrome are frequently reported to engage in topographies of physical aggression, such as grabbing or hair pulling (Summers, Allison, Lynch, & Sandler, 1995). Individuals with Angelman syndrome are reported to have a strong drive for social attention, and it has been noted that these specific topographies may be prevalent because they are likely to, at least temporarily, prolong social interactions (Oliver et al., 2007). As described above, hand biting is often described as being a characteristic behaviour in FXS. However, it would be of value to determine whether the combined evidence across all studies supports whether this topography of SIB is more common than others. In addition, there has been little exploration of topographical manifestations of other types of challenging behaviour, such as aggression. Understanding these patterns may have implications for future investigations and interventions.

Effective interventions for and prevention of behavioural challenges may be facilitated through understanding of the sources of motivation for the behaviour (Reiss & Havercamp, 1997). If particular genetic conditions are associated with motivational alterations, this may have several important implications. First, although not precluding the need for individualised assessments, such biases may direct clinicians as to which environmental influences to investigate as a priority. Second, knowledge of altered environmental influences upon behaviour support the development of preventive strategies, which are tailored to individuals with particular conditions. For instance, individuals with the condition could be proactively taught an adaptive response to ensure that they are able to access preferred reinforcement (such as attention for people with Angelman syndrome) appropriately. In addition, carers could be taught to ensure that their responses to challenging behaviours minimise inadvertent access to the potent reinforcer. Finally, if a motivational change is found to exist within FXS, then this supports the need for research to identify the internal causal mechanisms. The ability to then address aberrant motivations may then reduce the likelihood of individuals engaging in challenging behaviours.

Therefore, the aim of this review was to collate the existing data on the physical topographies and functions of challenging behaviours (including SIB, physical aggression, and destruction of property) displayed by individuals with FXS, in order to establish whether there is evidence to support the existence of within-group biases in the manifestation of challenging behaviours. The reason for this investigation is to guide future investigations into syndrome-specific influences upon challenging behaviour.

Method

Inclusion and exclusion criteria

Manuscripts written in English that included data on humans with a reported diagnosis of FXS were included in this systematic review. Where more detailed information was available on genetic status, individuals with mosaicism were included, but individuals were excluded if they were reported to have fewer than 200 CGG repeats in the FMR1 region (the diagnostic cut-off for FXS; Verkerk et al., 1991). Data regarding individuals with a diagnosis of a second genetic syndrome, in addition to FXS, were excluded. Individuals with a diagnosis of autism (in addition to FXS) were included due to a close association with FXS: Approximately 30% of individuals with FXS meet the diagnostic criteria for autism and many more exhibit behaviour characteristic of autism (see Hagerman, 2006, for a review). Due to various methods of assessing and reporting behaviours, it is not possible to report the prevalence of autism across the samples in this review. There was no minimum sample size for inclusion.

Topography studies

Studies were accepted that included information on the number of participants who engaged in SIB of a particular topography or directed at a particular body site. Studies investigating SIB were not included when they explicitly assessed for only one topography of SIB at a single body site, such as hand biting, as it was unclear whether either (a) the same topography of SIB could have also been directed at other body sites (such as biting lip); or (b) other topographies of SIB could have been directed at the same body site (such as skin picking on the hand). Studies were also included that reported the topography of physically aggressive behaviour or the topography of destructive behaviours (which may cause damage to the individual's physical environment, such as furniture).

Function studies

For data on function to be included, each participant was required to engage in at least one topography of challenging behaviour being addressed in the review (SIB, physical aggression, or property destruction). Evidence regarding behavioural function obtained by direct (experimental or observational) or indirect (validated questionnaire or interview) methods was included. Anecdotal evidence regarding behavioural function was excluded when it was not assessed via a validated indirect measure.

Literature search

A search string including variants on the terms "fragile X syndrome" and "challenging behaviour" was used. The string required papers to include at least one variant (using the "OR" command) of the term "fragile X syndrome" ("Martin-Bell" or "Escalante syndrome") and (using the "AND" command) at least one challenging behaviour–related term, which included: "challenging behaviour," "problem behaviour," "behaviour problems";

"maladaptive behaviour," "aberrant behaviour," "self-injurious behaviour," "self-injury; "self-harm," "aggression," "aggressive behaviour," "disruptive behaviour," "destruction of property," or "destructive behaviour." MeSH terms (in-built additional search vocabulary suggestions) were used where available in the database. Five databases were searched by the first author in June 2014: PsychINFO, PubMed, Web of Science, Autism Data, and SCOPUS. The initial search results yielded 768 papers overall including 525 individual documents.

Following abstract and title review, 176 articles were reviewed at the full-text stage. Reasons for exclusion included, but were not limited to, non-human subjects, lack of challenging behaviour data, articles in a language other than English, focus on fragile X pre-mutation carriers, and lack of fragile X–specific data (contact the authors for further details). The reference lists of the manuscripts reviewed at the full-text stage were scrutinised for additional relevant publications, leading to the identification of three additional resources. Finally, 18 manuscripts were identified that met the inclusion criteria for either the topography or function sections of the review. Reliability data for paper inclusion/exclusion was collected for 20% of the total papers, which were selected randomly. Agreement was scored if both raters excluded or included the paper. Initial agreement on final decisions was 95%. Where decisions were contradictory, the coders discussed and a mutual decision was reached.

Data extraction and analysis

Fifty percent of papers were independently assessed by a second rater to check the reliability of data extraction. Reliability was calculated according to agreement on number of individuals with challenging behaviour of a particular topography or function in each paper. Initial agreements on individual decisions were 100% for function data and 98.6% for topography data. Final decisions were reached collaboratively for items where raters disagreed.

Topography

Where information was available, data on the form (e.g., biting, scratching) of SIB and aggression, as well as the body site (e.g., hand, head) of SIB, was recorded. These data were used to calculate a total percentage of participants out of those who engaged in the relevant class of challenging behaviour (e.g., SIB), and who demonstrated a given topography of behaviour. The total percentages were calculated from the number of participants included in studies where the particular topography was assessed. Where a standardised measure was not used, for instance, in a caregiver interview prior to a functional assessment, it was assumed that all topographies of self-injury could have potentially been assessed. Measures used to assess topography are recorded in the tables in the Results section. Where a standardised measure was used but the results of all items were not presented, the authors were contacted to request further information. Additional unpublished data about behavioural topography was provided by Hessl et al. (2008).

Exact topographies were then grouped into categories for this review in order to be able to compare findings across studies. For instance, hitting self with body and hitting self with or against object were collapsed into self-injurious "hitting." Of note, topographies of behaviour were originally grouped differently across individual studies, leading to some uncertainty about the exact number of participants fitting into each review category. If clarification was unavailable after contacting the study authors, the available data were merged to best fit the study categories, acknowledging the potential variation in estimate that this may cause. Specifically, both the maximum and minimum prevalence of a class of behavioural topography (such as self-hitting) behaviours was calculated by assuming that cases of the subcategories of the behaviour (such as hitting self with body and hitting self against object) were either entirely non-overlapping (for instance, none of the participants who hit their bodies were the same as those who hit their heads) or overlapping (all of the participants who hit their bodies also hit their heads), respectively. These potential variations in prevalence estimates are represented as error bars on the graphs.

The topography of destructive behaviour was described for only 10 participants; therefore this information was not included in this manuscript. The information can be obtained through contact with the authors.

Function

Conclusions about behavioural functions made in studies were accepted. Where multiple assessments were conducted for an individual participant (e.g., a questionnaire measure and an experimental measure; Langthorne et al., 2011; Machalicek et al., 2014), the results of the direct measure were used when compiling the findings across studies. The exact functions from studies were noted, but in order to facilitate comparison across studies functions were also assigned to classes:

- Attention: The individual's behaviour was reported to be associated with the provision of attention.
- Social positive (other): The individual's behaviour was reported to be associated with the addition or increase of a reinforcer, other than attention alone, via another person. This included provision of tangible items or adult compliance with mands.
- Social negative: The individual's behaviour was reported to be associated with escape from or avoidance of a situation, such as the presentation of a demand, a social interaction, or a transition.
- Non-social: The individual's behaviour was reported to be associated with internal factors, such as pain or discomfort, or the behaviour itself appeared to be automatically positively reinforcing (indicated, for instance, by it occurring when the individual is alone).

As with the topography data, this classification resulted in some uncertainty as to the exact prevalence of behaviours serving each class of function, due to variation in categorisation of functions across different papers. Raw data from Langthorne and McGill (2012) was reanalysed to determine whether each participant showed any topography of behaviour with a particular function; in the original publication, the functions for different classes of challenging behaviour (SIB, aggression, and property destruction) were presented at the group level.

The aggregated data give information on the number of individuals with challenging behaviour, which at least partly maintained by a particular type of reinforcer. Where individuals had behaviours with multiple functions, they were counted in all relevant categories.

Data analysis

The statistical significance of prevalence differences was assessed using two-sided tests for the difference between proportions (Clarke & Cooke, 2004) in Microsoft Excel. Where there existed potential variations in the prevalence estimates, comparisons were conducted on the smallest possible difference in order to minimise Type II errors. Where nonsignificant findings were obtained, a second test was conducted using the maximum potential difference to evaluate the robustness of the finding. Unless otherwise reported, the comparisons yielded nonsignificant results for both the maximum and minimum differences.

Results of studies assessing the topography of self-injurious behaviour

Topography of self-injurious behaviour

Studies

Thirteen studies reported the topography of SIBs in males with FXS (see Table 1); two studies provided data for females (see Table 2). A variety of different measures were used to assess the topographies of SIBs (see Table 3). Studies explicitly assessing only hand biting were excluded from this analysis because it was unclear whether other participants may have also bit themselves at another body site, thus underestimating the overall prevalence of self-biting.

<<PLEASE INSERT TABLES 1, 2, AND 3 ABOUT HERE>>

Male summary

Across the studies, between 622 and 625 males with SIB were included. There were statistically significant differences between the proportions of males who were reported to show each of the four topographies of SIB, which were assessed in all studies. Biting was significantly more likely to be endorsed as being present than all other topographies (compared to hitting: $W = 10.09$, $N = 1{,}241$, $p < .0005$; Bonferroni adjusted alpha = .008); hitting was more likely to be rated as present than pulling ($W = 8.23$, $N = 1{,}241$, $p < .0005$) or scratching ($W = 6.03$, $N = 1{,}235$, $p < .0005$); there was no difference in the number of participants rated as engaging in pulling or scratching.

Female summary

In total, fewer different topographies of SIB were assessed in females with FXS; therefore the prevalence of other topographies of SIB (such as teeth-grinding, vomiting, and pica) is unclear. Percentages of the four topographies of SIB, which were assessed in both studies, are displayed alongside the male data in Figure 1. Unlike males with FXS, there were no significant differences between the proportions of those assessed who engaged in the different topographies of SIB.

Gender comparisons

There was no significant difference between the proportion of males or females who self-scratched or self-hit. In contrast, males were significantly more likely to self-bite than females (Bonferroni alpha = 0.125; minimum difference: $W = 2.54$, $N = 678$, $p = .011$; maximum difference: $W = 4.01$, $N = 678$, $p < .001$). In addition, a higher percentage of females self-picked compared to males (maximum difference: $W = 3.24$, $N = 678$, $p < .005$). However, comparisons using the minimum potential difference did not reach significance according to the adjusted alpha level ($W = 2.48$, $N = 678$, $p = .013$). Thus, this trend towards gender differences in SIB topography is not statistically robust (see Figure 1).

<<PLEASE INSERT FIGURE 1 ABOUT HERE>>

Body sites towards which self-injurious behaviour is directed

Studies

Seven studies included data on the body sites of male participants' self-injurious behaviour (see Table 4) and one for females (Symons, Byiers, Raspa, Bishop, & Bailey, 2010). All studies were deemed to have potentially assessed SIB in all body sites. Studies reporting the prevalence of hand biting in individuals with FXS were excluded from this analysis due to uncertainty about whether other topographies of SIB were also directed at the hand.

Summary

As reported by Symons and colleagues (2010), who investigated 51 females with SIB, the most common body site for SIB in females is towards the arm or hand (75.5%), followed by the head (51%), legs or feet (30.6%), then torso (18.4%). Similarly, in the total sample of males assessed across the six studies (between 481 and 488 individuals), SIB was significantly most commonly towards the hand or arm followed by the head ($W = 11.61$, $N = 969$, $p < .0005$; Bonferroni adjusted alpha = .008). More male participants injured their head than their legs ($W = 10.66$, $N = 969$, $p < .0005$) or torsos ($W = 9.81$, $N = 976$, $p < .0005$); there was no significant difference in the number of males with FXS who directed their SIB to their legs or torsos.

Gender comparisons

Gender differences for head, arm, and torso were not significant. A higher proportion of females injured their legs than males (Bonferroni adjusted alpha = .0125; $W = 2.3$, $N = 532$, p

= .05), but this was significant only when the largest potential difference was considered (W = 2.59, N = 539, p < .01).

Results of studies reporting the topography of aggressive behaviours

<<PLEASE INSERT TABLE 4 ABOUT HERE>>

Studies

Eight studies gave details of the topographies of physically aggressive behaviours shown by males with FXS (see Table 5). No studies provided comparable data for females.

<<PLEASE INSERT TABLE 5 ABOUT HERE>>

Summary

In the total sample of males with FXS and aggressive behaviours (69 individuals), there was a significant difference in the number of participants (based upon minimum estimates) who engaged in different topographies of aggression. In order to minimise the number of comparisons, statistical differences were only investigated between the four most common topographies of aggression. A significantly higher proportion of individuals were reported to hit, compared to other topographies of aggression (Bonferroni adjusted alpha = .008; compared to kicking: W = 3.3, N = 138, p < .001).

Results of studies assessing the function of challenging behaviours

Studies

The function of challenging behaviours shown by individuals with FXS (including at least one topography of either SIB, aggression, or property destruction) was assessed in 10 studies (see Table 6) using a variety of direct and indirect measures. Many researchers assessed the operant function of multiple topographies of behaviour in a single assessment. Therefore, it was not possible to assess the function of each type of challenging behaviour separately, based on the data available.

<<PLEASE INSERT TABLE 6 ABOUT HERE>>

Summary

The results of individual studies can be seen in Table 6 and are compared overall in Figure 2. Of the 94 boys studied (age 22 months to 22 years), 24 or 25 engaged in challenging behaviour at least partly maintained by access to attention (only 11 were reported to engage in these behaviours in a 1:1 scenario, the remainder did so only when the other individual's attention was being divided with a third person); 55 engaged in challenging behaviours maintained by another source of social-positive reinforcement besides attention; between 70 and 74 engaged in challenging behaviours maintained at least partly by social-negative reinforcement; finally, the behaviour of 21 participants was at least partly maintained by non-social sources of reinforcement. Visual analysis supported that, all included cases different assessment types yielded similar proportions classes of social function, though the non-social results differed widely (see Figure 3).

<<PLEASE INSERT FIGURES 2 AND 3 ABOUT HERE>>

Social-negative reinforcement was significantly the most common category (Bonferroni adjusted alpha = .008; compared to social positive [other], which was the next most common category: $W = 2.82$, $N = 188$, $p < .005$). A significantly higher proportion of participants was reported to have challenging behaviours that served a function in the social-positive (other) category, compared to attention ($W = 5.65$, $N = 188$, $p < .0005$) or non-social ($W = 6.39$, $N = 188$, $p < .0005$). There was no significant difference between the frequency of non-social and attention functions.

Discussion

We collated the existing data on the topography and function of challenging behaviours displayed by people with FXS in order to provide new insights into influences upon behaviour within the syndrome.

Across the studies reporting SIB topography in males with FXS, biting was the most common topography of the behaviour. Although, interestingly, females with FXS were not more likely to self-bite, compared to other topographies of SIB. Furthermore, gender differences could be seen in the proportion of those with SIB who showed this topography: a higher proportion of males self-bit than females. Regarding the body location of SIBs, across all participants, these behaviours were commonly directed at the hands or arms. This pattern of body sites may be a secondary result of the tendency to self-bite, as there are limited body areas (presumably, arms, hands, lips, cheeks, or tongue) that can be easily targeted by self-biting without requiring high response-effort. Therefore, the data suggesting within-syndrome patterns of SIB topography are partially consistent with the idea that self-biting is a phenotypic feature. However, this aggregated information highlights a potential gender difference in the manifestation of SIB in FXS. To the authors' knowledge, no researchers have investigated gender differences in the topographies of SIBs more generally; therefore it is unclear whether these differences represent a general trend or are related specifically to the gender differences in FXS, resulting from being an X-linked condition.

The definition of a behavioural phenotype is that a behaviour is more common in individuals with a condition relative to those without (Dykens, 1995), meaning that comparison with results from other populations will strengthen the assertions that such patterns of behaviour may be phenotypic. In Richards, Oliver, Nelson, and Moss's (2012) cross-condition comparison, included in this review, males with FXS showed a significantly higher relative risk of engaging in self-biting when compared with individuals with either autism spectrum disorder (2.52 times more likely) or Down syndrome (7.67 times more likely). These findings, along with the within-group comparison in this review, support the notion that self-biting forms part of the behavioural phenotype of males with FXS. However, no researchers have conducted a comparison of SIB body sites between individuals with and without FXS, and there is a paucity of research with comparable populations investigating body sites of SIB against which the present findings could be compared. Future research involving comparisons of females with FXS to matched samples and group comparisons of SIB body sites would be required to strengthen the investigation of SIB manifestation in FXS.

With regard to the topography of aggressive behaviour, the available information suggests that hitting is the significantly most common topography displayed by males with FXS. No studies have directly investigated the prevalence of different topographies of aggression between individuals with FXS and a comparison group. However, comparison of this data with research with other groups reveals similar patterns: hitting was found to be the most common topography of aggression in samples of individuals with mixed aetiology ID (Emerson & Bromley, 1995; Sigafoos, Elkins, Kerr, & Attwood, 1994) and a sample of individuals with cri du chat syndrome (Collins & Cornish, 2002). Therefore, it does not appear that this expression of physical aggression is unique to males with FXS. Previous studies have noted that aggression may be clinically significant for some females with FXS (e.g., Hessl et al., 2001), although there is little information to describe how this manifests.

Next, the results of the review of studies investigating behavioural function are discussed. Within the group of young males with FXS assessed in this research, challenging behaviours were significantly more likely to serve an escape or avoidance (social negative) function, compared to any other class of function. This suggests that the motivation to escape from or avoid situations may be elevated in males with FXS. When the specific functions assigned to the category of social-negative reinforcement are analysed more closely, escape-maintained challenging behaviours appeared to be most closely associated with the presence of demands or transitions. Interestingly, despite the high levels of social anxiety and socially avoidant behaviours associated with FXS (Cordeiro et al., 2011), escape from social interactions did not appear to be a particularly common function for challenging behaviour: only four out of the 19 participants who participated in an experimental functional analysis, which included a test for a social-escape function, showed elevated levels of target behaviours in this condition. Furthermore, low levels of attention-maintained behaviours were observed in this review; social positive (attention) was the joint least common class of function for challenging behaviours. This reflects earlier suggestions that the motivation to access adult attention may be diminished in FXS, even if levels of challenging behaviour to escape from ongoing interactions may not be elevated (e.g., Langthorne et al., 2011).

Comparisons of behavioural function between FXS and individuals without the condition allow assessment of whether this pattern of behavioural function is "phenotypic." Langthorne and colleagues (Langthorne & McGill, 2012; Langthorne et al., 2011) compared males with FXS to other groups (Smith−Magenis syndrome and non-specified ID), finding that the FXS participants were significantly less likely to engage in attention-maintained behaviour. Furthermore, our aggregated findings regarding behavioural function appear to differ in pattern from the pattern of functions seen across a review of all published experimental functional analyses. Beavers and colleagues (2013) found that, of those assessments that were differentiated, 32% of participants' behaviours served a demand-escape function, compared to a higher proportion of 59% in this review (of participants with FXS who partook in an experimental functional analysis). This supports that the individuals with FXS in our sample may have been relatively more likely to engage in escape-maintained behaviour than other populations engaging in challenging behaviours. In addition, only 13% of the FXS participants showed elevated levels of problem behaviour in the attention condition of a functional analysis, compared to 21.7% in Beavers et al.'s review. This finding corresponds to the within-group observation that the probability of this function may be lowered. However, it is worth considering that Beavers and colleagues assigned results to function categories according to single functions, whereas in the present review functions were categorised by behaviours that were at least in part maintained by a particular reinforcer, which may limit the comparability of these findings.

Taken together, the joint consideration of within-syndrome findings and the comparison with results from other populations suggests that there may be motivational changes associated with FXS that influence the operant learning of challenging behaviours: the motivation for negative social reinforcement is elevated relative to the motivation for positive reinforcement through the provision of attention. These findings have implications for the intervention and prevention of challenging behaviours in FXS. For instance, early training might focus upon teaching communicative behaviours to request negative reinforcement (such as a break from a task) in order to provide functional alternatives to escape-maintained challenging behaviours prior to their development. Future researchers should investigate behavioural function in females with FXS, to determine the applicability of these findings to that group.

It is currently unclear from the available data whether specific behaviours exhibited by individuals with FXS are more likely to be associated with certain functions. Langthorne and McGill (2012) conducted separate indirect functional assessments for self-injury, aggression, and property destruction. Visual analysis suggests that aggression was more likely to serve an escape function than self-injury; however, the significance of this difference was not evaluated. In the future, researchers might investigate, for instance, whether phenotypic behaviours, such as hand biting, are more likely to be associated with a given function compared to other behaviours. Understanding topography-function relationships may have implications for future analysis and treatment.

There are several limitations with this review that warrant consideration when interpreting the findings. First, by bringing together the results of different studies for analysis, the implicit assumption was made that the heterogeneous measures used corresponded highly to each another. We recognise, however, that the definitions of behaviours differ between studies and different measures, which may limit their comparability. A review of the validated measures of behavioural topography revealed relatively subtle differences in the wording of descriptions of behaviour. However, where a validated measure was not used, it was not clear what questions were asked and whether this may have affected the response.

The assumption of the compatibility of findings via different measures may be particularly challenged in the case of the data regarding function of challenging behaviours, as data show poor correspondence between the outcomes of direct and indirect methods of assessment (Toogood & Timlin, 1996). Comparison of the proportions of different social outcomes (i.e., attention, other social positive, escape) reported from direct and indirect measures of behavioural function across the FXS sample suggest that there is not a significant difference in the likelihood of each measurement type yielding each type of social function. However, the results of indirect measures were more likely to report non-social functions than direct assessments. This particular difference may be influenced by the fact that Machalicek and colleagues (2014) did not include a “no interaction” condition in their experimental analysis, meaning that they may have not been able to adequately detect non-social functions for behaviour. The participants in this study constitute almost half of those (47.8%) who participated in a direct functional assessment. Of note, four of these 11 individuals were reported to have automatically reinforced (non-social function) behaviour in an indirect parental assessment. Therefore, this poor correspondence for non-social functions between assessment types may result from variation in individual study methodologies. Of note, the correspondence of direct and indirect measure within studies was mixed, including for social functions (Langthorne et al., 2011; Machalicek et al., 2014). Therefore, it is possible that had all of the participants been assessed using the same measure, a different pattern of results may have been seen. Furthermore, the results of the functional assessments were only validated by the implementation of function-based interventions for seven participants, all of which were successful at reducing target behaviours (Hagopian, Toole, Long, Bowman, & Lieving, 2004; Joy, 2009; Moskowitz, Carr, & Durand, 2011; O'Connor, Sorensen-Burnworth, Rush, & Eidman, 2003; O'Reilly, Lancioni, King, Lally, & Dhomhnaill, 2000); this equates to 7.4% of the total sample in this review. Information on behavioural function was obtained through direct assessment for four of these participants and indirect for three. Without validation through implementation, it is unclear whether the conclusions about function were valid, although earlier research has demonstrated the validity of both direct and indirect functional assessments more broadly. A suggestion for future research is to investigate the utility of functional approaches to behavioural intervention in FXS by assessing the success of function-based treatments for challenging behaviours, based upon both direct and indirect assessment findings.

A further limitation with the review is that there may have been small errors in the calculation of numbers of participants who engage in specific behaviours. First, as acknowledged previously, by combining the data into groups, some uncertainty was created about the exact number of participants to be assigned to each group owing to unknown overlap of participants. Minor mistakes may have also occurred in calculating the numbers of participants to be placed in each category for the review due to the calculation of numbers of participants from percentages provided in publications. In addition, where behaviour was assessed by parent report or clinical assessment, it was assumed that all topographies of behaviour could potentially have been assessed. It is possible, however, that there may have been reporting biases. For instance, only highly visible behaviours may have been detected by a clinician or behaviours of the highest concern may have been prioritised for assessment, leading to the underreporting of other topographies of behaviour. In addition, given the earlier suggestion of the specific association between FXS and hand biting, this topography of behaviour may have been more readily reported.

A further methodological consideration with this review is that studies investigating hand biting only were excluded due to the separation of body location and topographical analyses. This approach allowed for the amalgamation of the greatest proportion of relevant manuscripts. However, the excluded papers may have influenced the findings of this investigation. Finally, it is unclear whether the observed patterns were confounded by the inclusion of participants with a dual diagnosis of autism. A project explicitly examining challenging behaviours in individuals with FXS, with and without a diagnosis of autism, and those with nonsyndromic autism, would help to clarify this issue.

This review has provided new insights into challenging behaviour associated with FXS. The next steps from this review will be to use this knowledge to steer the investigations into influences upon challenging behaviours in FXS. Physiological hyper-arousal is believed to contribute to the FXS behavioural phenotype (Cohen, 1995). This is supported by evidence suggesting that FXS is associated with atypical activity in the endocrine stress system: the limbic hypothalamic-pituitary-adrenal (L-HPA) axis (Hessl et al., 2002). It is possible that changes in the body's stress-related physiology in FXS may be associated with the observed patterns of behaviour in this review. Of note, there is some evidence that chewing during acute stress is associated with a subsequent smaller L-HPA stress response (Allen & Smith, 2011), providing a potential link between arousal and biting. In addition, Langthorne and colleagues (2011) have suggested that changes to the stress response may underpin the motivational changes, such as desire to escape from "stressful" demands in FXS. Therefore, in addition to the suggestions for future research mentioned above, investigations of the relationship between indicators of arousal and challenging behaviours, including hand biting, in FXS under a range of environmental conditions seem warranted.

Conclusion

In this review, we have systematically brought together the findings of studies of challenging behaviour displayed by individuals with FXS. Comparisons within the studied groups of individuals with FXS support the existence of a bias towards particular topographies and functions of challenging behaviours within the condition, at least for males. Future research should include samples of females with FXS, involve comparisons with other groups, and investigate influences upon behaviour in FXS, such as aberrant stress-related arousal.

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Table 1. Individual study and review findings regarding the topography of SIBs in males with fragile X syndrome.

Study	Study *N* with SIB	Number of participants with each topography of SIB											
		Hitting self (with body or with/against object)	Biting self	Pulling or picking (hair/skin)	Rubbing/ scratching	Inserting objects into body openings	Teeth grinding	Extreme liquid drinking	Aerophagia (excessive air swallowing)	Vomiting	Pica	Pulling nails	Pinching
Hagerman (2002)	1	0	1	0	0	0	0	0	0	0	0	0	0
Hagopian et al. (2004)	1	1	1	0	0	0	0	0	0	0	0	0	0
Hall et al. (2008)	18	5	14	1	7	0	–	–	–	–	–	–	–
Hessl et al. (2008)[a]	40	25	15	4–7	13–6	3–6	13–5	7–10	1–4	7–10	9–12	5–8	4–7
Langthorne et al. (2011)	8	6	1	0	0	0	0	0	0	0	0	0	0
Largo & Schinzel (1985)	5	1	4	0	0	0	0	0	0	0	0	0	0
Levitas et al. (1983)	6	–	5	1	–	–	–	–	–	–	–	–	–
Machalicek et al. (2014)	6	5	3	0	0	0	0	0	0	0	0	0	0
Moscowitz et al. (2011)	3	1	2	0	0	0	0	0	0	0	0	0	0
Richards et al. (2012)	67	49	59	18	18	10	–	–	–	–	–	–	–
Sheldon & Turk (2000)	2	2	2	0	0	0	0	0	0	0	0	0	0
Symons et al. (2003)	32	13–19	23–25	11	6	2	–	–	–	–	–	–	–
Symons et al. (2010)	433–6	171–2	301–3	112	130–1	–	–	–	–	–	–	–	–
Minimum total	622	261	430	147	174	15	12	7	1	7	9	5	4
Maximum total	625	286	435	150	178	18	15	10	4	10	12	8	7
Minimum proportion of those assessed for SIB topography (%)		42.2	68.8	23.5	28.1	8.2	18.2	10.6	1.5	10.6	13.6	7.6	6.1
Potential estimate variation (+%)		4.2	1.1	0.6	0.8	1.6	4.5	4.5	4.5	4.5	4.5	4.5	4.5

Note. – = Not assessed in study.

[a]Additional unpublished data provided.

Table 2. Individual study and review findings regarding the topography of SIBs in females with fragile X syndrome.

Study	Study *N* with SIB	Number of participants with each SIB topography			
		Hitting	Biting	Pulling/picking (hair/skin)	Rubbing/scratching
Hall et al. (2008)	5	0	2	1	4
Symons et al. (2010)	48–51	25–27	24–26	20–21	15–16
Total	53–56	25–27	27–29	21–22	19–20
Minimum proportion of those assessed for SIB topography (%)		44.6	48.2	37.5	33.9
Potential estimate variation (+%)		6.3	6.5	4.0	3.8

Table 3. Measures used to assess SIB topography.

Study	Measure used to assess topography of SIB
Hagerman (2002)	Clinical examination
Hagopian et al. (2004)	Parent report (functional analysis)
Hall et al. (2008)	Self-Injury Checklist (Bodfish, Crawford, Powell, & Parker, 1995)
Hessl et al. (2008)	Behavior Problems Inventory (BPI; Rojahn, Matson, Lott, Esbensen, & Smalls, 2001)
Langthorne et al. (2011)	Clinical examination (parent report prior to functional analysis)
Largo & Schinzel (1985)	Clinical examination
Levitas et al. (1983)	Clinical examination
Machalicek et al. (2014)	Clinical examination (parent report prior to functional analysis)
Moskowitz et al. (2011)	Parent Functional Assessment Interview
Richards et al. (2012)	Challenging Behaviour Questionnaire (Hyman, Oliver, & Hall, 2002)
Sheldon & Turk (2000)	Clinical examination
Symons et al. (2003)	Self-Injury Questionnaire based upon Functional Assessment Interview (O'Neill et al., 1990)
Symons et al. (2010)	Self-Injury Questionnaire based upon Symons et al. (2003)

Table 4. Individual study and review findings regarding the body location of SIBs in males with fragile X syndrome.

Study	Assessment method	*N* with SIB	Number of participants with SIB at body location			
			Head	Hand/arm	Leg/feet	Torso
Hagerman (2002)	Clinical examination	1	0	1	0	0
Hagopian et al. (2004)	Clinical examination	1	1	1		
Langthorne et al. (2011)	Clinical examination	8	2	6		
Machalicek et al. (2014)	Clinical examination	6	5	3	0	0
Moskowitz et al. (2011)	Clinical examination	3	1	2	1	
Sheldon & Turk (2000)	Clinical examination	2	2	2		
Symons et al. (2003)	Self-Injury Grid (Symons & Thompson, 2003)	32	20	19–32	6	5
Symons et al. (2010)	Based upon Symons et al. (2003)	436	198	348	70	89
Totals		489	229	395	77	94
Minimum proportion SIB at body location (%)			46.83	77.91	15.75	19.22
Potential estimate variation (+%)			0	2.87	0	0

Table 5. Individual study and review findings regarding the topography of physically aggressive behaviours in males with fragile X syndrome.

Study	Assessment method	Participants with aggression	Number of participants with topography of physical aggression							
			Hitting	Kicking	Grabbing/ pulling	Spitting	Pinching	Pushing	Biting	Scratching
Hagerman (2002)	Clinical examination	1	1	1	0	0	0	0	0	0
Hagopian et al. (2004)	Clinical examination	1	1	1	1	0	0	0	0	0
Hessl et al. (2008)	Clinical examination	38	24	22	23–6	12–5	13–6	17–20	7–10	10–13
Langthorne et al. (2011)	Clinical examination	8	7	2	2	1	1	1		1
Largo & Schinzel (1985)	Clinical examination	7	5	0	0	0	0	0	2	0
Machalicek et al. (2014)	BPI[b]	10	7	4	1	0	1	1	3	0
Moscowitz et al. (2011)	Clinical examination	3	1	1	2	0	0	1	0	0
O'Reilly et al. (2000)	Clinical examination	1	0	0	0	0	1	1	0	0
Total across studies:		69	46	31	29–32	13–6	16–9	21–4	12–5	11–14
Minimum proportion of participants with aggression showing the topography (%)			66.7	44.9	42.0	18.8	23.2	30.4	17.4	15.9
Potential estimate variation (+%)			0.0	0.0	4.3	4.3	4.3	4.3	4.3	4.3

Table 6. The function of challenging behaviours of individuals with fragile X syndrome.

Study	Total participants	Functional assessment method	Class of behavioural function	Number of participants	Detail about behavioural function	Number of participants
Hagopian et al. (2004)	1 male	Direct (Experimental functional analysis; Iwata, Dorsey, Slifer, Bauman, & Richman, 1982/1994)	Social positive (attention)	1	Access to adult attention	1
			Social positive (other)	1	Access to tangible items	1
			Social negative	1	Termination of "do requests"	1
					Escape from demands	1
Langthorne et al. (2011)	8 males	Direct (Experimental functional analysis)	Social positive (other)	4	Access to tangible items	4
			Social negative	5	Escape from social interaction	1
					Escape from demands	4
Machalicek et al. (2014)	11 males*	Direct (Experimental functional analysis)	Attention	3	Access to mother's attention	3
			Social positive (other)	10	Access to tangible items	10

			Social negative	10	Escape from social interaction	3
					Escape from demand	8
O'Reilly et al. (2000)	1 male	Direct (Brief experimental functional analysis)	Attention	1	Access to attention when parents are interacting with a third person	1
O'Connor et al. (2003)	1 male	Direct (Experimental functional analysis, followed by pairwise mand analysis; Bowman, Fisher, Thompson, & Piazza, 1997)	Social positive (other)	1	Adult compliance with mands	1
Joy. (2009)	1 male[b]	Direct (Naturalistic pairwise analysis comparing routine interactions with a familiar person to novel interactions)	Attention	1	Gain reactions from mother and sister	1
			Social negative	1	Escape from play with sister	1
					Escape novel social interactions	1
Hills Epstein, Riley, & Sobesky (2002)	1 male	Direct (Non-specified observational assessment)	Social positive (attention)	1	Access to mother's attention when frustrated with an object or bored with a situation	1

Langthorne & McGill (2012)	35 males	Indirect (Questions About Behavioral Function [QABF]; Matson & Vollmer, 1995)	Attention	4	Access to attention	4
			Social positive (other)	20	Access to tangible items	20
			Social negative	22	Escape from demands	22
			Non-social	16	Pain related	9
					Automatic reinforcement	12
Moscowitz et al. (2011)	3 males	Indirect (Parent interview; Contextual Assessment Inventory [CAI]; McAtee, Carr, Schulte, & Dunlap, 2004) and Functional Assessment Interview (FAI; O'Neill et al., 1997)	Attention	1	Access to mother's attention	1
			Social negative	3	Delaying going to bed	1
					Escape from novel or unpredictable places	1
					Escape from the toilet	1
Symons et al. (2003)	32 males	Indirect (Questionnaire based on the FAI. Parents	Attention	12–13	Access to attention	1

asked to rate if challenging behaviour was more likely to occur before, during or after a given series of situations)			Access to attention when others' attention is divided with a third person	12
	Social positive (other)	19	Access to tangible items	19
	Social negative	28–32	Following changes in routine	28
			Following presentation of a command	21
			Following a difficult task	20
			Following interruption of a preferred routine	18
	Non-social	5	When left alone	5

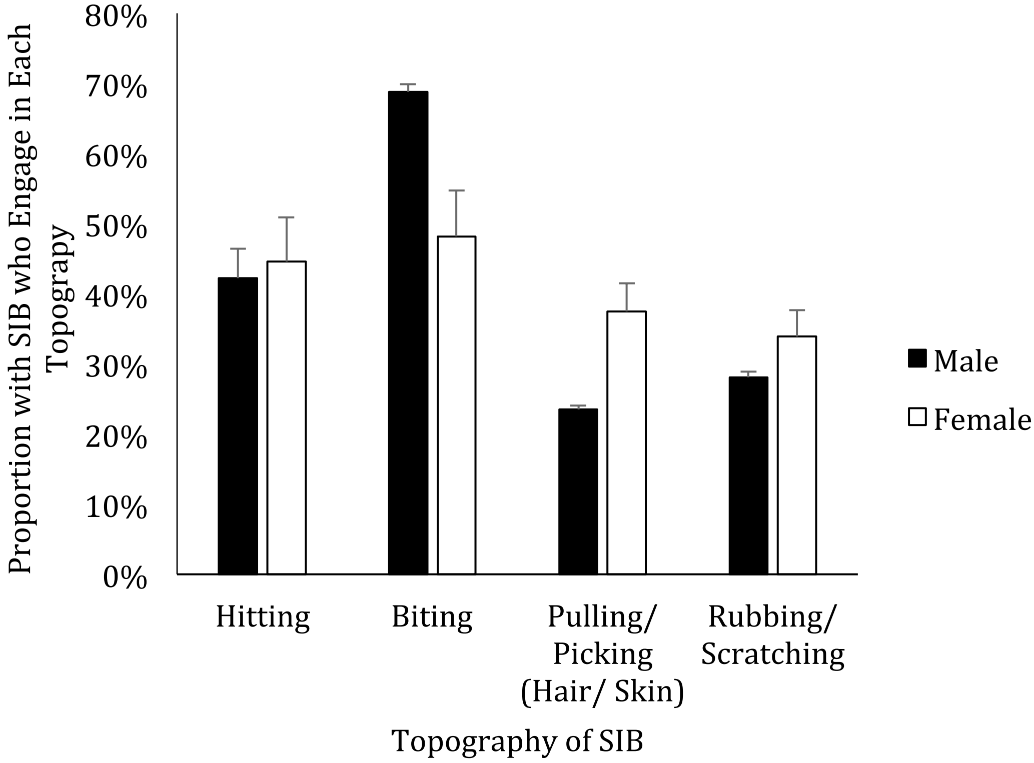
[b]One participant excluded because target behaviours in functional assessment did not include any topographies of self-injury, physical aggression, or property destruction.

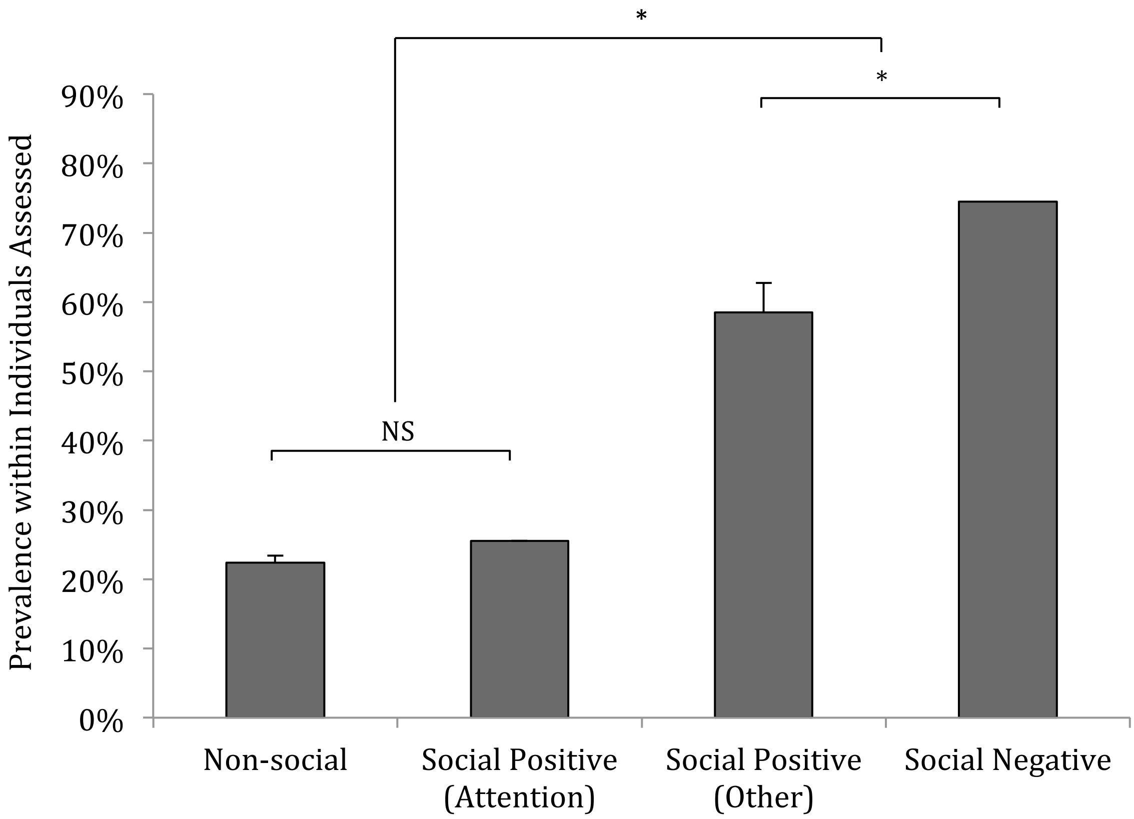
FIGURE CAPTIONS.

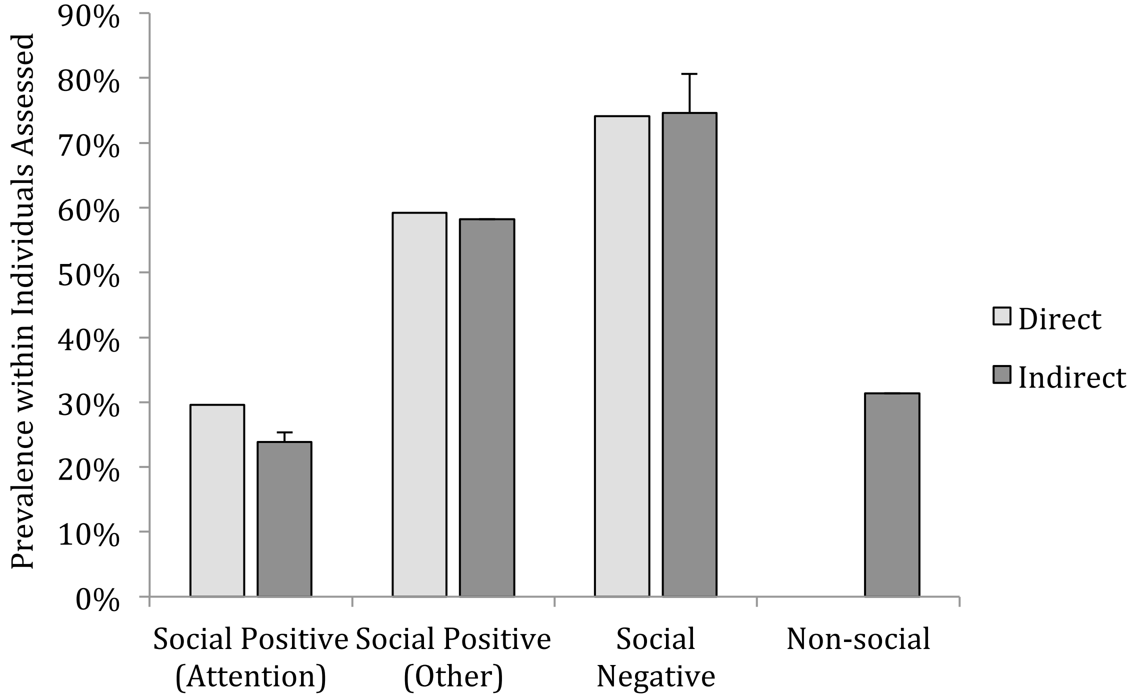
Figure 1. A comparison of SIB topography of males and females with FXS.

Figure 2. Proportion of individuals with FXS whose challenging behaviour was found to be at least partly maintained by each class of reinforcement. *Denotes significant difference ($p <$ .008). NS signifies nonsignificant difference ($p \geq .008$). Error bars represent maximum prevalence estimate.

Figure 3. Categorised results of functional assessments via direct and indirect methodologies.


Proportion with SIB who Engage in Each Topograpy
80%
70%
60%
50%
40%
30%
20%
10%
0%
Hitting
Biting
Pulling/ Picking (Hair/ Skin)
Rubbing/ Scratching
Topography of SIB
Male
Female


*
*
NS
Prevalence within Individuals Assessed
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Non-social
Social Positive (Attention)
Social Positive (Other)
Social Negative


90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Prevalence within Individuals Assessed
Social Positive (Attention)
Social Positive (Other)
Social Negative
Non-social
Direct
Indirect