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Review article

The prevalence of aggression in genetic syndromes: A review

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ABSTRACT

Research into behavioural phenotypes identifies both environmental and organic factors as influencing aggression in children and adults with genetic disorders associated with intellectual disability. However, in contrast to self-injury there is a paucity of research that compares aggression across relevant syndromes. The primary aim of this review is to examine the association between aggression and genetic syndromes by analysis of prevalence studies. The review also examines the literature on the form of the behaviour and influence of environmental factors.

Results imply that certain syndrome groups (Cri du Chat, Smith-Magenis, Prader-Willi, Angelman, Cornelia de Lange, and Fragile X syndromes; estimates over 70%) evidence a stronger association with aggression than others (e.g. Williams and Down syndromes; estimates below 15%). However, the strength of association is difficult to quantify due to methodological differences between studies. The results from examining form and environmental influences highlight the importance of phenotype–environment interactions. Research employing group comparison designs is warranted and future work on the assessment and intervention of aggression in genetic syndromes should consider the importance of phenotype–environment interactions.

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Aggression in individuals with intellectual disability (ID) impinges on quality of life, carer well being, and contributes to the breakdown of residential placements (Hastings, 2002; Tausig, 1985). Prevalence estimates for aggression in ID vary widely, in part because of methodological differences (Borthwick-Duffy, 1994; Harris & Russell, 1989; Quine, 1986; Sigafoos, Elkins, Kerr & Atwood, 1994). A recent review of prevalence studies of aggression in ID that limited inclusion to those reporting 'physical aggression', suggested rates of physical aggression in ID are likely to lie at the upper end of the widely cited 2–20% estimate (Davies & Oliver, 2013). For example, Tyrer et al. (2006) and Crocker et al. (2006) examined prevalence in over 3000 individuals with ID and reported overall rates of 14% and 24.4% respectively. Similarly, Smith, Branfield, Collacot, Cooper, and McGrother (1996) reported a prevalence of 22% in 2202 adults with ID. Relative risk analyses of studies reporting prevalence across age groups has indicated that aggression increased with age until mid-adulthood (Davies & Oliver, 2013).

A robust and diverse research literature highlights the importance of environmental factors generally, and operant theory specifically, in the development and maintenance of aggression. It has been demonstrated repeatedly in experimental studies that such behaviours can be sensitive to, and maintained by socially, and non-socially mediated forms of reinforcement such as attention or the presentation of tangible items from carers (Carr & Durand, 1985), and removal of task demands (Iwata, Pace, Kalsher, Cowdery, & Cataldo, 1990). In a review of functional analytic studies, Hanley, Iwata, and McCord (2003) demonstrated that in 50 of 52 studies, aggression was mediated by an operant reinforcement process.

Although operant theory has significant empirical support, there is a broad consensus that biological factors also play a role in behaviours such as self-injury and aggression (e.g. Arron, Oliver, Moss, Berg, & Burbridge, 2011; Langthorne & McGill, 2012; May et al., 2009). Certain syndrome groups evidence a comparatively higher prevalence of self-injury, aggression, and destructive behaviour than others, and forms of behaviour also differ across genetic syndromes (Arron et al., 2011).

In addition to syndrome related associations, certain person characteristics are known to be associated with aggression. McClintock, Hall, and Oliver (2003) found that Autism Spectrum Disorder (ASD), Attention-Deficit/Hyperactivity Disorder (ADHD), being male, and reduced communication skills were all associated with aggression. Within genetic syndromes, Arron et al. (2011) found that impulsivity and over-activity were significantly higher in participants showing aggression than in those who did not. Furthermore, in studies examining risk factors for aggression in ASD, lower IQ, poorer expressive and receptive language, and repetitive behaviours have been identified as associated with aggression (Dominick, Davis, Lainhart, Tager-Flusberg, & Folstein, 2007; Kanne & Mazurek, 2011).

Evidence from the operant and behavioural phenotype literatures suggest that both environmental and organic factors may play a role in the manifestation of aggression in genetic syndromes (see Oliver et al., 2013; Tunnicliffe & Oliver, 2011). However, there is a paucity of research that directly compares aggression across syndromes, and this is in contrast to the literature on self-injury. This lack of research is surprising given that many of the risk factors known to be associated with aggression (i.e. impulsivity, over-activity, repetitive behaviours, ASD, and reduced communication abilities) are frequently described in certain genetic syndromes (e.g. Clarke & Boer, 1998; Finucane, Konar, Haas-Givler, Kurtz, & Scott, 1994; Hagerman, 2002; Oliver, Berg, Burbidge, Arron, & Moss, 2011). Identification of increased risk for aggression would facilitate the implementation of early intervention strategies to reduce or replace behaviours before they become established. Furthermore, as it has been suggested that successful interventions require knowledge of underlying operant influences (Harvey, Boer, Meyer, & Evans, 2009) it is necessary to investigate the role of environmental influences on aggression across syndromes.

This review will examine the extent to which aggression is associated with specific genetic syndromes by analysis of studies that report the prevalence of aggression in these groups. This will ascertain whether certain syndromes show a heightened association with aggression in comparison to others. The review will then examine the literature outlining the form of the behaviour in these groups, and literature that examines the influence of environmental factors on aggression.

1. Method

1.1. Selecting syndromes for inclusion

1.1.1. Search strategy

Due to the number of syndromes that might potentially be investigated, screening was undertaken to identify which syndrome groups were reported in research papers relevant to the review. A search using Ovid PsychInfo was conducted on

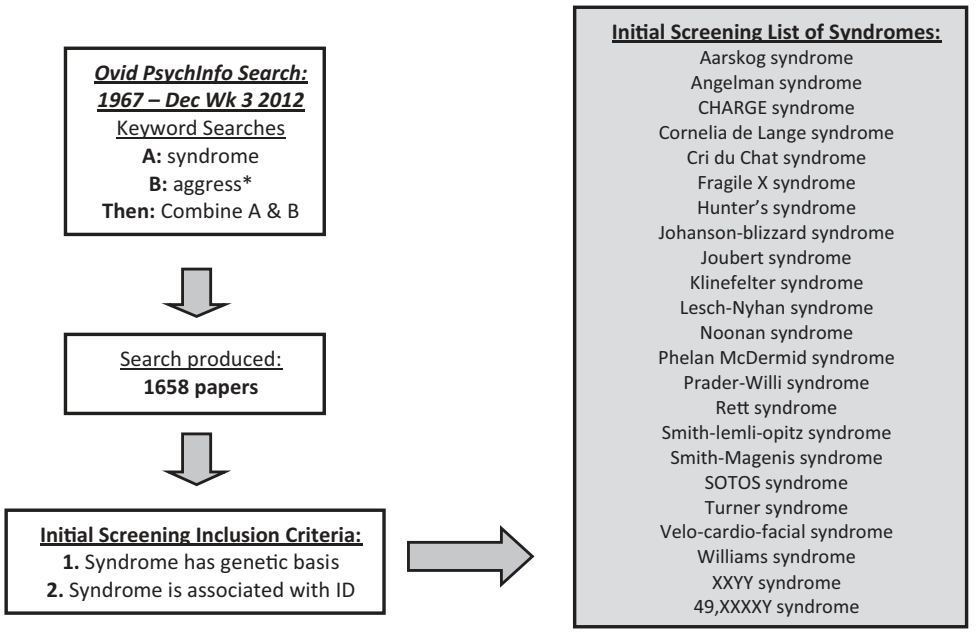

Fig. 1. Initial screening search.

papers between 1967 – December Week 3, 2012. The search strategy, including inclusion criteria, is presented in Fig. 1. As expected, results included a number of syndromes that did not have a genetic basis or were not associated with ID (e.g. restless leg syndrome, Tourette's syndrome). Consequently, only syndrome groups with a known genetic basis that were associated with ID were included in the screening list, this was determined by reviewing empirical papers that documented these characteristics in the groups.

The search was then broadened by combining each syndrome name with the word 'behavio*' to identify any papers documenting specific topographies of aggression (e.g. hit, kick) that would be omitted if the search was restricted to 'aggress*'. Syndromes were then selected by examining the number of papers reporting prevalence figures for a sample of 20 participants or more. As there is no single definition of aggression used consistently, any paper that reported a prevalence of 'aggress*' or a particular topography of aggression (punching, pushing, kicking, tripping, pulling hair, scratching, throwing objects, using objects as weapons, grabbing clothing) was included. Finally, syndromes were included only if there was more than one paper estimating prevalence. Consequently, seven syndromes were selected for review: Fragile X (FXS), Prader-Willi (PWS), Smith-Magenis (SMS), Williams (WS), Angelmans (AS), Cri du Chat (CdCS), and Cornelia de Lange (CdLS). In addition to the papers identified by Ovid PsychInfo, a hand search was conducted for each syndrome to locate papers not highlighted by the electronic review. The search strategy, including inclusion criteria, is presented in Fig. 2.

Down syndrome (DS) was not included as part of the systematic review. DS is a well-documented genetic syndrome with a comparatively clearly defined behavioural phenotype that could serve the purpose of a well-defined contrast group with which to compare prevalence rates across other syndromes. Due to the extensive literature available for DS, using the same search term used for the other groups (i.e. 'behavio*') would have yielded vast numbers of papers not applicable to the current review. Therefore a different search strategy was adopted to constrain search findings to those of most relevance. The search strategy, including inclusion criteria, is presented in Fig. 3.

1.2. Syndromes included for review

1.2.1. Cri du Chat syndrome

CdCS has an estimated prevalence of approximately 1 in 50,000 live births (Niebuhr, 1978), and is predominately caused by a deletion on the short arm of chromosome 5, with a critical region of 5p15 (Wu, Niebuhr, Yang, & Hanson, 2005). A de novo deletion is present in 85% of cases, and 10–15% of cases are familial (Van Buggenhout et al., 2000). Behaviours noted to occur in CdCS include self-injurious behaviour, repetitive behaviour, obsessive attachment to objects, sleep problems, hypersensitivity to sensory stimuli, and aggressive and destructive behaviour (Clarke & Boer, 1998; Collins & Cornish, 2002; Van Buggenhout et al., 2000).

1.2.2. Smith-Magenis syndrome

SMS has a reported prevalence of between 1 in 25,000 live births (Greenberg et al., 1996), and 1 in 15,000 (Laje et al., 2010). Typically, the syndrome results from a de novo deletion on chromosome 17 (17p11.2) (Girirajan et al., 2006) but for approximately 10% of cases, a mutation of the retinoic acid-induced 1 (RAI1) gene on the same chromosome has been

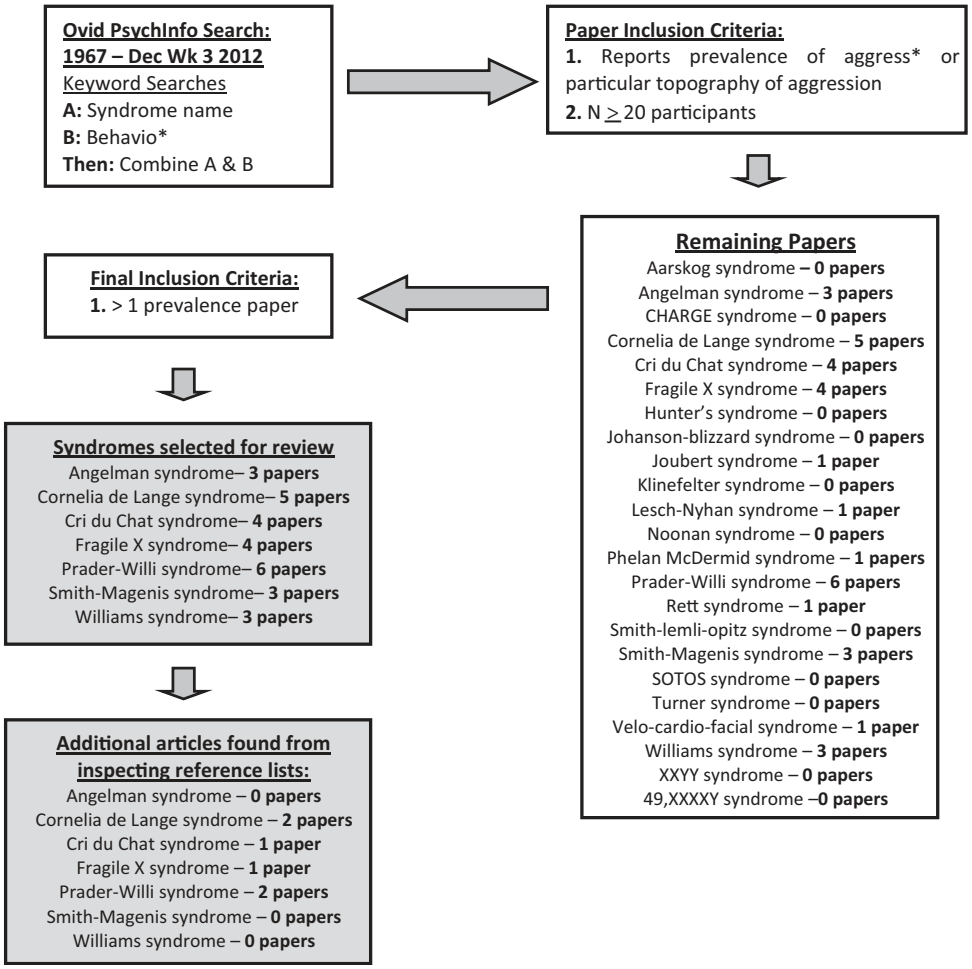

Fig. 2. Search strategy.

implicated (Elsea & Girirajan, 2008). Self-injurious behaviour has been noted frequently (e.g. Smith et al., 1986), along with sleep difficulties, aggressive behaviour, restlessness, distractibility, hyperactivity, autistic features, and a unique 'self hug' (Finucane et al., 1994).

1.2.3. Fragile X syndrome

FXS is the most common inherited form of ID with a prevalence of approximately 1 in 3600 males and 1 in 8000 females (Turner, Webb, Wake, & Robinson, 1996). Genetic basis involves the expansion of a trinucleotide repeat sequence,

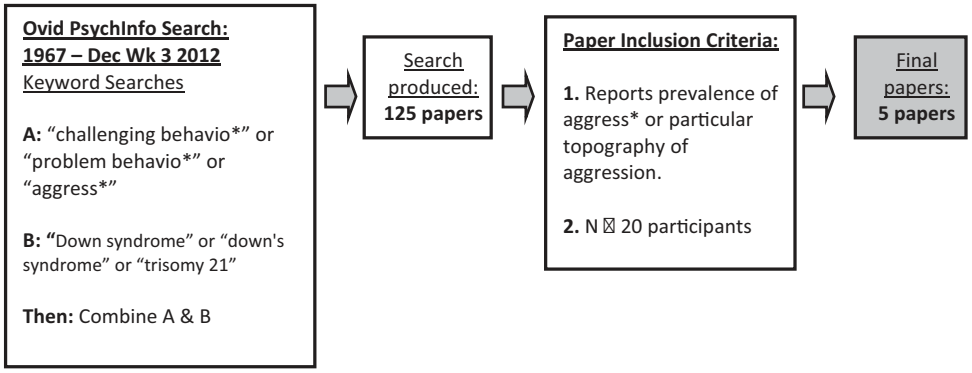

Fig. 3. Search strategy for Down syndrome (DS).

cytosine-guanine-guanine (CGG), in the promoter region of the FMR1 gene located at Xq27.3 of the long arm of the X chromosome (Sansone et al., 2012). In addition to ID, research suggests a specific behavioural phenotype characterised by aggression, inattention, hyperactivity, and ASD behaviours (Hagerman, 2002; Hatton et al., 2002; Sullivan et al., 2006).

1.2.4. Angelman syndrome

AS has a reported prevalence of approximately 1 in 52,000 live births (Õiglane-Shlik et al., 2006). AS results from the absence of maternally derived genetic material on chromosome 15 in the region of 15q11–q13 but there are several different genetic mechanisms. In a small proportion of cases, AS results from either a paternal uniparental disomy (UPD; 4–7% of cases), a UBE3A gene mutation (10% of cases), or imprinting centre deficits (3–4% of cases). However, in the majority of cases (approximately 70%), AS is caused by maternal deletions of chromosome 15q11–q13 (Dagli, Buiting, & Williams, 2012; Ludwig et al., 2005). The behavioural phenotype of AS is characterised by a strong drive for adult attention, and high levels of laughing and smiling behaviours (e.g. Horsler & Oliver, 2006; Oliver, Demetriades, & Hall, 2002). Other notable behaviours include sleep difficulties (Bruni et al., 2004), hyperactivity, and inattentive behaviour (Clarke & Marston, 2000; Summers & Feldman, 1999).

1.2.5. Cornelia de Lange syndrome

CdLS has a reported prevalence of between 1 in 10,000 and 1 in 50,000 live births (Beck & Fenger, 1985; Opitz, 1985). Approximately 60% of cases result from a mutation on the NIP-BL gene (5p13.1), but other mechanisms including mutations on chromosome 10 (SMC3 gene) and X-linked SMC1A and HDAC8 genes have been implicated (Deardorff et al., 2012; Musio et al., 2006). The behavioural phenotype includes self-injurious behaviours, hyperactivity, and repetitive behaviours (Arron et al., 2011). A heightened prevalence of autistic-like characteristics has been identified (Moss, Howlin, & Oliver, 2011), and anxiety, social impairments, and low mood have been described in adolescents and young adults (in press, citation withheld for blind review).

1.2.6. Prader-Willi syndrome

PWS has a reported prevalence of approximately 1 in 52,000 live births (Whittington et al., 2001), and is caused by either a paternal deletion (e.g. larger Type I versus smaller Type II deletions) within the 15q11–q15 region (approx. 70%), or by maternal uniparental disomy (UPD) of chromosome 15 (Cassidy & Driscoll, 2009). Characteristic behaviours include hyperphagia, temper tantrums, impulsivity, skin picking, repetitive speech, stubbornness, and aggression (Dykens & Cassidy, 1995; Dykens & Kasari, 1997; Einfeld, Smith, Durvasula, Florio, & Tonge, 1999; Greenswag, 1987).

1.2.7. Williams syndrome

WS has a reported prevalence of 1 in 7500 live births (Stromme, Bjornstad, & Ramstad, 2002), and is caused by the microdeletion of approximately 25 genes on the long arm of chromosome 7 (Donnai & Karmiloff-Smith, 2000). The most widely documented behaviours associated with the WS phenotype include heightened sociability, increased empathy, and anxiety (Dykens, 2003; Udwin & Yule, 1991). Challenging behaviours such as aggression do not typically form part of the behavioural phenotype and thus have not been widely examined.

1.2.8. Down syndrome

DS is the most common cause of ID associated with a chromosomal anomaly, with an estimated prevalence of 1 in every 732 live births when averaged across maternal ages (Canfield et al., 2006). In the vast majority of cases, the syndrome results from non-disjunction involving chromosome 21 during meiosis, but a small proportion of cases are mosaic in nature or caused by a translocation of genetic material between chromosome 21 and another chromosome (Connor & Ferguson-Smith, 1997). Typically, individuals with DS display fewer behavioural problems than individuals with other causes of ID (Dykens, 2007).

2. Results

2.1. Prevalence of aggression in selected syndromes

The studies outlining prevalence data for each syndrome group are presented in Table 1 together with information regarding the studies' aims, recruitment strategy, methodology, definition, time period, age of sample, and sample size. The review identified 39 papers reporting the prevalence of aggression. For CdCS, five papers were identified with estimates ranging from 18.5% to 88%; SMS, three papers (57–87.5%); FXS, five papers (14–75%); AS, three papers (10–73%); CdLS, seven papers (7.4–75%); PWS, eight papers (10.4–73%); WS, three papers (6.7–15%) and finally, for DS, five papers (3.7–12%).

2.1.1. Comparison of prevalence across genetic syndromes

Fig. 4 presents a visual representation of the prevalence rates reported for each syndrome group. Median values and number of studies per group are also displayed. The highest prevalence rate was reported for CdCS at 88%, and the lowest rate was for DS at 3.7%.

Table 1
The prevalence of aggression in genetic syndromes.

	Author	Study aims	Recruitment	Method	Definition used to report prevalence of aggression	Time period	Mean age (range)	*N*	Prevalence
CdCS									
CdCS	Cornish and Pigram (1996)	To assess the developmental and behavioural characteristics of 27 children with CdCS	UK Syndrome support group	Parents completed The Society for the Study of Behavioural Phenotypes Postal Questionnaire	1. 'Physically aggressive to family members'	Not given	8.3 years (4–16)	27	1. 33.3%
					2. 'Physically aggressive to non family members'				2. 18.5%
CdCS	Dykens and Clarke (1997)	To examine the range, distinctiveness and correlates of maladaptive behaviour in individuals with CdCS	US and UK syndrome support groups	Parents completed The Aberrant Behavior Checklist-Community	'Aggressive to others' (verbally or physically)	1 month	12.0 years (2–40)	146	70%
CdCS	Cornish et al. (1998)	To extend knowledge of the behavioural phenotype of CdCS to include a profile of a young cohort's adaptive and maladaptive functioning	UK syndrome support group	Parents were interviewed using The Vineland Adaptive Behavior Scales, Interview Edition (includes a 'maladaptive behaviour' section)	'Too physically aggressive'	'Current'	7.6 years (4–16)	49	30%
CdCS	Collins and Cornish (2002)	To determine the prevalence and frequency of stereotypy, self-injurious behaviour, and aggression in children and adults with CdCS	UK syndrome support group	Parents completed The Behavior Problems Inventory (BPI)	Prevalence reported based on 'informant responded to at least one item on this subscale'. Items on the aggressive/destructive subscale included: hitting others with hand or body part; hitting others with objects; meanness or cruelty; biting others; scratching others; pinching others; and destructive behaviour	Rated between 'less than monthly to 'hourly'.	14.75 years (6–37)	66	88%
CdCS	Arron et al. (2011)	To examine the prevalence and associated characteristics of self injurious and aggressive behaviour in seven genetic syndromes	Syndrome support group	Parents completed The Challenging Behaviour Questionnaire (CBQ)	'Physical aggression' (e.g. punching, pushing, kicking, pulling hair, grabbing other's clothing)	1 month	17.20 years	58	70.2%
SMS									
SMS	Dykens and Smith (1998)	To examine the distinctiveness and correlates of maladaptive behaviour in 35 children with SMS	Syndrome support group and syndrome conference	Parents completed The Child Behavior Checklist (CBCL)	Prevalence reported as 'physical aggression' but exact CBCL items used were not specified	6 months	9.00 years	105	57%

SMS	Arron et al. (2011)	To examine the prevalence and associated characteristics of self injurious and aggressive behaviour in seven genetic syndromes	Syndrome support group	Parents completed The Challenging Behaviour Questionnaire (CBQ)	'Physical aggression' (e.g. punching, pushing, kicking, pulling hair, grabbing other's clothing)	1 month	15.45 years	42	73.8%
SMS	Sloneem et al. (2011)	To investigate the prevalence and phenomenology of aggressive behaviour in SMS	UK syndrome support group	Parents were interviewed using the Challenging Behaviour Interview (CBI)	'A non-accidental, physical act involving physical contact with another person likely to result in pain or distress. Examples: punching, pushing, kicking, tripping, pulling hair, scratching, throwing objects, using objects as weapons, and grabbing clothing'	1 month	15.09 years (6–39)	32	87.5%
FXS									
FXS	Sarimski (1997a)	To explore the behavioural phenotypes of three genetic syndromes	German syndrome support group	Parents completed the Society for the Study of Behavioural Phenotypes Postal Questionnaire (SSBPQ)	Prevalence reported as 'physically aggressive' but exact SSBPQ items used were not specified	Not given	84.3 months	30 males	40%
FXS	Hatton et al. (2002)	To examine the problem behaviour over time in boys with FXS	Genetic clinics, developmental evaluation centres, and early intervention programs	Parents completed the Child Behavior Checklist (CBCL)	Prevalence reported based on 'Aggressive behaviour' domain score being in the 'borderline or clinical range'. The CBCL Aggressive Behavior domain includes various constructs including: arguing, meanness, destruction of property and jealousy	6 months	86.60 months (48–152)	59 males	17%
FXS	Bailey et al. (2008)	To report the frequency of selected co-occurring conditions in individuals with variations in the FMR1 gene	Three FXS Foundations	Informant report via telephone or web-based questionnaire	''Has this child ever been diagnosed with or treated by a medical professional for any of the following conditions?'' 'Aggressiveness towards others' was listed	'Ever'	Not specified	976 males	38%
								259 females	14%
FXS	Hessl et al. (2008)	To examine whether the 5-HTTLRP and MAOA-VNTR polymorphisms are associated with severity of behavioural problems in FXS	Two referred due to concerns about aggression. All others were sequential clinic referrals	Parents completed The Behavior Problems Inventory (BPI)	Prevalence reported based on 'aggression towards others' but exact BP1-01 items used were not specified	2 months	15.6 years (8–24)	50 males	75%
FXS	Arron et al. (2011)	To examine the prevalence and associated characteristics of self injurious and aggressive behaviour in seven genetic syndromes	Syndrome support group	Parents completed The Challenging Behaviour Questionnaire (CBQ)	'Physical aggression' (e.g. punching, pushing, kicking, pulling hair, grabbing other's clothing)	1 month	16.57 years	191 males	52%.

Table 1 (*Continued*)

	Author	Study aims	Recruitment	Method	Definition used to report prevalence of aggression	Time period	Mean age (range)	*N*	Prevalence
AS									
AS	Zori et al. (1992)	To further delineate the clinical and developmental features of Angelman syndrome	UK Syndrome Support Group and USA Research Group	Parents completed 'a general developmental questionnaire'	Prevalence reported based on 'aggressive behaviour' but further definition not provided	Not given	Not given	66	10.6%
AS	Summers et al. (1995)	To examine the nature and prevalence of behaviour problems among clients with Angelman syndrome	Medline literature search of case reports from 1965 to 1992	Review of 34 case reports	Prevalence reported based on 'aggression' but further definition not provided	Not given	Not given	108	10%
AS	Arron et al. (2011)	To examine the prevalence and associated characteristics of self injurious and aggressive behaviour in seven genetic syndromes	Syndrome support group	Parents completed The Challenging Behaviour Questionnaire (CBQ)	'Physical aggression' (e.g. punching, pushing, kicking, pulling hair, grabbing other's clothing)	1 month	13.40 years	104	73%
CdLS									
CdLS	Gualtieri (1991)	Investigation into behaviour in the CdLS	USA syndrome support group	Parents completed a questionnaire about medical background, family history, drug treatment, and abnormal behaviours	Prevalence reported based on 'been aggressive at one time or another' but further definition not provided	'At one time or another'	10.4 years (1–39)	78	73%
CdLS	Sarimski (1997b)	To survey the social–communicative abilities and behavioural abnormalities in CdLS	German syndrome support group and from an existing database from previous assessment	Parents completed The Behavior Problems Inventory (BPI) and The Society for the Study of Behavioural Phenotypes Postal Questionnaire (SSBPQ)	1. BPI prevalence reported based on informant endorsing 'biting, hair pulling or beating others' as 'a problem'	Rated between 'monthly' to 'hourly'	7.1 years (1–16)	27	7.4%
					2. SSBPQ prevalence reported on informant endorsing 'attacking other people'	Not given			7.4%
CdLS	Berney et al. (1999)	To further delineate the behavioural phenotype of CdLS	UK Pediatrics, clinical genetics, child psychiatry and syndrome support group	Parents completed The Society for the Study of Behavioural Phenotypes Postal Questionnaire (SSBPQ)	Prevalence reported as 'aggression' but exact SSBPQ items used were not specified	At least occasionally	Not given	49	1. 75%
						At least daily			2. 49%

CdLS	Hyman et al. (2002)	To examine the range of challenging behaviours in CdLS, with a focus on SIB and self restraint	UK syndrome support group	Caregivers were asked via a questionnaire whether the individual 'had shown physical aggression in the last month'	Physical Aggression was defined as any punching, pushing, kicking, pulling hair, throwing objects, or grabbing other's clothing	1 month	12.89 years (1–38)	88	43.2%
CdLS	Basile, Villa, Selicorni, and Molteni (2007)	To provide greater insight into the clinical, behavioural and cognitive characteristics associated with CdLS	Clinic referrals and Italian Syndrome support group	Parents completed The Developmental Behaviour Checklist – Primary Career Version (DBC-P).	Prevalence reported as 'aggressiveness' but exact DBC-P items used were not specified	6 months	10.58 years (1–31)	56	20%
CdLS	Arron et al. (2011)	To examine the prevalence and associated characteristics of self injurious and aggressive behaviour in seven genetic syndromes	Research database	Parents completed The Challenging Behaviour Questionnaire (CBQ)	'Physical aggression' (e.g. punching, pushing, kicking, pulling hair, grabbing other's clothing)	1 month	17.49 years	101	40.2%
CdLS	Rojahn et al. (2012)	To validate the Behavior Problem Inventory-01 in a population of individuals with CdLS	USA syndrome support group	Parents completed The Behavior Problems Inventory (BPI)	Prevalence based on 'informant responded to at least 1 item on aggressive/destructive subscale'. Items included: Hitting, kicking, pushing, biting, and scratching others; grabbing and pulling, bring verbally abusive, destroying things, and being mean or cruel	Rated between 'monthly' to 'hourly'	16.8 years (1.5–61.4)	180	70.5%
PWS									
PWS	Sarimski (1997a)	To explore the behavioural phenotypes of three genetic syndromes	German syndrome support group	Parents completed The Society for the Study of Behavioural Phenotypes Postal Questionnaire	Prevalence reported as 'physically aggressive' but exact SSBPQ items used were not specified	Not given	80.2 months	35	11.4%
PWS	Boer and Clarke (1999)	To describe the developmental and behavioural aspects of PWS	UK syndrome support group	Parents completed The Society for the Study of Behavioural Phenotypes Postal Questionnaire	'Aggressive towards'				
PWS	Einfeld et al. (1999)	To determine PWS has increased psychopathology compared to controls	Australian Hospital Genetics Register	Parents completed The Developmental Behaviour Checklist – Primary Career Version (DBC-P)	1. Children Prevalence reported based on number of informants who endorsed 'kicks, hits others' on the DBC-P	Not given 6 months	(3–51) years 17.7 years	205 75	1. 10.7% 41%

Table 1 (*Continued*)

	Author	Study aims	Recruitment	Method	Definition used to report prevalence of aggression	Time period	Mean age (range)	*N*	Prevalence
PWS	Wigren and Heimann (2001)	To relate differences in patterns of skin picking to prevalence of compulsive and impulsive-aggressive behaviours	Swedish syndrome support group	Parents completed a questionnaire 'designed for the purpose of capturing specific features relevant to PWS'	Prevalence reported based on 'tantrums including violent acts against persons, for example, hitting, kicking, spitting or pinching'	Rated between 'once a year' to "once a week"	20.6 years (12–30)	37	49%
PWS	Holland et al. (2003)	To report the behavioural differences between PWS and learning disabilities, and the prevalence of these behaviours	Research database and syndrome support group	Informant based interviews utilising a diagnostic checklist to establish the presence/absence of clinical characteristics	Prevalence reported based on 'definite or some violent or aggressive outbursts'	Not given	20.8 years	91	73%
PWS	Hartley et al. (2005)	To further define significant differences in maladaptive behaviours among the typical deletion and UPD subtypes of PWS, and determine if subject characteristics are significant correlates	Not given	Parents completed The Reiss Screen for Maladaptive Behaviour (RSMB)	Prevalence reported based on 'aggressive behaviour' subscale score being above the clinically significant range	3 months	23.81 years (12–45)	1. 65 (total) 2. 41 (deletion) 3. 23 (UPD)	1. 39.7% 2. 47.5% 3. 26%
PWS	Hiraiwa et al. (2007)	To test whether behavioural and psychiatric disorders intensified with age in PWS	Japanese syndrome support group	Parents completed a questionnaire asking whether their child had showed a number of behavioural problems	Prevalence reported based on the number of informants answering 'yes' to "Has your child shown aggressive behaviour in the last five years"?	5 years	(2–31) years	165	32%
PWS	Arron et al. (2011)	To examine the prevalence and associated characteristics of self injurious and aggressive behaviour in seven genetic syndromes	Syndrome support group	Parents completed The Challenging Behaviour Questionnaire (CBQ)	'Physical aggression' (e.g. punching, pushing, kicking, pulling hair, grabbing other's clothing)	1 month	17.04 years	571	43%
WS									
WS	Gosch and Pankau (1997)	To determine whether individuals with WS show differences in aspects of personality and rates of behavioural problems at different ages	Syndrome Association National Conference and German Syndrome support group	Parents completed the Child Behavior Checklist (CBCL)	Prevalence reported based on number of informants who endorsed 'hits others'	6 months	169.7 months (27–424)	105	6.7%

WS	Sarimski (1997a)	To explore the behavioural phenotypes of three genetic syndromes	German syndrome support group	Parents completed The Society for the Study of Behavioural Phenotypes Postal Questionnaire	Prevalence reported as 'physically aggressive' but exact SSBPQ items used were not specified	Not given	74.4 months	35	8.6%
WS	Papaeliou et al. (2012)	To provide a comprehensive account of the behavioural profile of Greek young children with WS	Not given	Parents completed the Child Behavior Checklist (CBCL)	Prevalence reported based on the 'Aggressive behaviour' domain score being in the 'borderline or clinical range'. The CBCL Aggressive Behavior domain includes various constructs including: arguing, meanness, destruction of property and jealousy	6 months	61.5 months	20	15%
DS									
DS	Collacott, Cooper, Branford, and McGrother (1998)	To examine the behavioural characteristics of a substantial and unselected cohort of adults with DS	National Health Service Records, Social Services, & Care Homes	Parents responded to the Disability Assessment Schedule (DAS) Interview	Prevalence reported as 'aggression' but exact DAS items used were not specified	Not given	37.14 years	360	8.6%
DS	Tyrer et al. (2006)	To report on the prevalence of physical aggression towards other people in adults with LD living in Leicestershire	Leicestershire LD Register	Parents responded to the Disability Assessment Schedule (DAS) Interview	Prevalence reported based on if respondent reported aggression was 'severe and occurred frequently (>3 times a week)' or was 'severe in nature but occurred less frequently'; or considered to be 'less severe but occurred frequently (> three times a week)'	12 months	Not given as DS included as part of larger study	502	6.0%
DS	Dykens, Shah, Sagun, Beck, and King (2002)	To examine age-related changes in the maladaptive behaviour of children and adolescents with DS	Syndrome support group and clinic for people with DS	Parents completed the Child Behavior Checklist (CBCL)	Prevalence reported as 'engaging in physically aggressive acts' but exact CBCL items used were not specified	6 months	9.74 years	211	12%
DS	Van Gameren-Oosterom et al. (2011)	To investigate the development, problem behaviour, and health-related quality of life in a sample of Dutch children with DS at the age of 8 years old	Dutch syndrome support group	Parents completed the Child Behavior Checklist (CBCL)	Based on the 'aggressive behaviour' domain being in the 'clinical range'. The Aggressive Behaviour domain includes various constructs including: arguing, meanness, destruction of property and jealousy	6 months	8.14 years (7.8–9.1)	325	4.4%
DS	Hattier, Matson, Belva, and Kozlowski (2012)	To investigate the effects of diagnostic group and gender on challenging behaviours in infants and toddlers with cerebral palsy, DS, or seizures	Via an early intervention project	Parents responded to the Baby and Infant Screen for Children with Autism Traits-Part 2 (BISCUIT)	Prevalence reported based on number of informants who endorsed 'physically cruel to people or animals'	Not given	Not given as DS included as part of larger study	27	3.7%

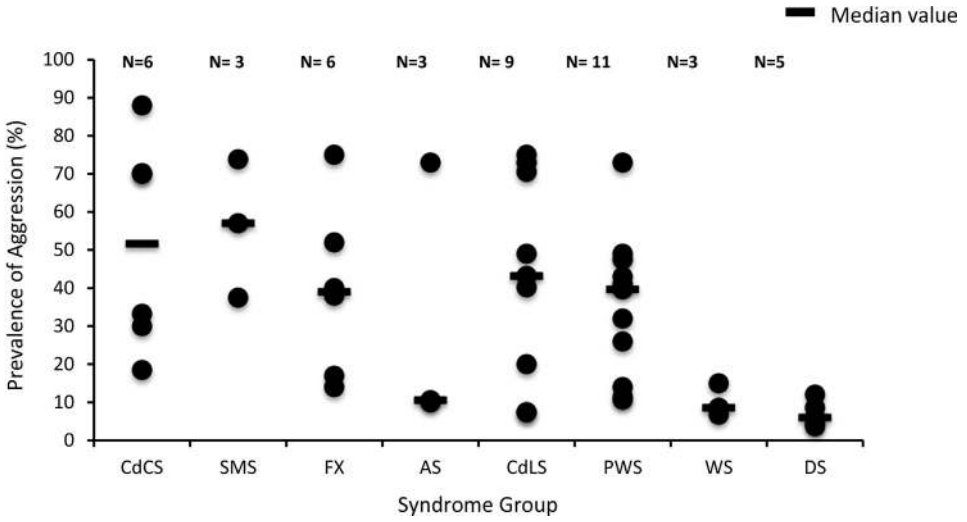

Fig. 4. Percentage prevalence rates of aggression across genetic syndromes.

The prevalence rates for aggression in DS and WS are consistently low. For these two groups, prevalence estimates cluster closely together and all lie below 15%, with median values of 8.6% and 6% for WS and DS respectively. These results are perhaps unsurprising given that the research literature for these two groups suggests that challenging behaviour does not constitute part of the behavioural phenotype (Dykens, 2003, 2007). In contrast, the prevalence rates reported for the other syndrome groups include very high estimates. Although the highest estimate of 88% is reported in CdCS; the SMS, FXS, AS, CdLS, and PWS groups all have estimates above 70%. When these estimates are compared to the estimates reported for DS and WS, and the estimates of around 20% given in total ID population studies (Crocker et al., 2006; Davies & Oliver, 2013; Smith et al., 1996; Tyrer et al., 2006), the prevalence of aggression appears higher in these groups. However, the range of estimates for these groups is very large. Not only does this variability make it difficult to ascertain the degree to which aggression is associated with each group, it also makes drawing comparisons between groups difficult. Such variation may result from the methodological differences that exist between studies.

2.1.2. Methodological influences on prevalence estimates

One of the main methodological issues is 'case' ascertainment. Methods include: a review of case studies, standardised informant questionnaires and interviews, and non-standardised questionnaire measures. It is possible that certain methods, such as the Challenging Behaviour Interview (CBI; Oliver et al., 2003) as used by Sloneem, Oliver, Udwin, and Woodcock (2011) for SMS, may yield larger estimates because it does not constrain report on predetermined behaviours. In contrast, other methods such as a review of case studies as used by Summers, Allison, Lynch, and Sandler (1995) may yield lower estimates. Although case studies can offer important information, they are often based on global impressions rather than systematic measurement (Dykens, 1995). Summers et al. (1995) drew attention to this limitation and concluded that behavioural problems may have been under reported due to case studies focussing predominately on diagnostic and management issues.

The definition and time period used for case ascertainment also varies. Across studies, the time periods used vary from 'ever' to 'daily'. The impact of such variation can be demonstrated by considering four of the studies reporting prevalence for CdLS. Both Gualtieri (1991) and Berney, Ireland, and Burn (1999) used a broad time period when asking about aggression in CdLS ('at any time in the past' and 'at least occasionally' respectively), and produce estimates above 70%. In contrast, Arron et al. (2011) and Hyman, Oliver, and Hall (2002) asked whether aggression occurred 'in the last month', and produce estimates below 45%. The use of a broad time period means that less frequent behaviours are also included resulting in higher estimates. Indeed, when Berney et al. (1999) reduced the time period from 'at least occasionally' to 'at least daily', prevalence rates dropped from 75% to 49%.

The definitions used across studies vary widely between structured and clear behavioural descriptions as used by Sloneem et al. (2011) for SMS; to the use of subjective statements such as 'too physically aggressive' as used by Cornish, Munir, and Bramble (1998) for CdCS; or the use of subscales that combine two separate constructs such as the 'aggressive/destructive subscale' used by Collins and Cornish (2002) for CdCS. The use of different definitions has a significant effect on the spread of prevalence rates reported. For example, it could be that some individuals with CdCS in the Cornish et al. (1998) study *did* show aggression but subjectively were not considered as '*too* aggressive', and consequently this could yield a comparatively lower prevalence rate. This possibility seems likely given that the same author conducted a similar study four years later (recruiting via the same UK parent support group) yet reported a much higher prevalence rate when the prevalence was derived from a subscale that combined two separate constructs – aggression and destruction. The issue of subjectivity is also important when interpreting the prevalence rates for AS. The prevalence rate reported by Arron et al. (2011) is approximately seven times higher than the rates reported by the other two studies. This difference is striking but

when considered alongside the terms and definitions used by the three studies, highlights an important point. When parents are asked about aggression, it is likely that they typically interpret the term as it is used in common usage, where an intent to harm is implicit. This is particularly relevant in AS where the behavioural phenotype is characterised by a strong desire for adult interaction (e.g. Horsler & Oliver, 2006). Even though forms of aggressive behaviour may be present, parents may often feel that the person they care for does not intend to harm and so do not label these behaviours as aggressive. Such subjectivity does not arise when individual forms of behaviour are specified. Therefore, it is possible that the much higher prevalence rate reported by Arron et al. (2011) results because the Challenging Behaviour Questionnaire (CBQ; Hyman et al., 2002) defines operationally, and so is not as influenced by inferring intent.

The effect of age, gender, and genetic-subtype differences on prevalence estimates within and between studies also requires attention. Evidence suggests that these factors are related to the prevalence of aggression, and therefore should be considered when interpreting the estimates provided in this review.

The studies in the review differ widely with regard to age range. Some studies recruit children only whereas others recruit across the lifespan. This is relevant as it has been suggested that aggression increases with age until mid-adulthood in people with ID (Davies & Oliver, 2013). Similarly, evidence suggests aggression may differ across ages within syndrome groups. Arron et al. (2011) found aggression was more likely to occur in younger than older individuals with CdCS, FXS, and PWS a pattern not evident other syndromes. Furthermore, Hartley, MacLean, Butler, Zarcone, and Thompson (2005) suggest that adults with PWS in their twenties were more likely to show aggressive behaviour than adolescents and older adults, and Hiraiwa, Maegaki, Oka, and Ohno (2007) suggest a trend towards more problem behaviours in PWS with age.

Although gender differences for aggression in ID have been described previously (McClintock et al., 2003), the majority of estimates reported in this review are based on mixed gender samples, and potential gender differences are not considered. However, the study by Bailey, Raspa, Olmsted, and Holiday (2008) for FXS can be used to highlight the importance of considering gender differences. Studies have shown that males and females with FXS can vary widely in the extent of intellectual impairment, with females typically being less severely affected than males (Loesch, Huggins, & Hagerman, 2004). Such male–female differences are thought to be due to cellular mosaicism and X inactivation (Migeon, 2006). Although there are no studies with which to compare, the results by Bailey et al. (2008) suggest lower rates of aggression in females. It is important to note that this difference in aggression in FXS females may be attributable to level of ID rather than to gender difference per se, but nonetheless demonstrates the importance of moving away from mixed gender samples and towards the consideration of within syndrome difference.

Consideration of the potential impact of within syndrome genetic-subtype differences on aggression is lacking. Although some syndromes in the review arise from various different genetic mechanisms, rates are reported for the entire syndrome group rather than for each genetic subtype. This is important when considering that phenotypic presentations may differ between genetic subtypes. For example in AS, emerging evidence suggests that individuals with the paternal UPD may have a milder phenotypic presentation (Bottani et al., 1994). It is currently unclear whether a milder phenotypic presentation might be associated with higher or lower levels of aggression. However, one possibility might be that higher ability levels could enable an individual to be more physically capable of instrumental aggression.

Another important methodological consideration to note relates to the recruitment methodology used across studies. The vast majority of studies recruit participants via syndrome support groups. It is possible that families and carers are more likely to access support if they care for a person showing challenging behaviour. Therefore, the estimates reported in these studies may be elevated and unrepresentative of the wider population. Also, a number of the studies included in the review recruited via the same support groups and therefore the different studies may contain the same participants. This is especially likely in the studies outlining prevalence of aggression in CdCS as all five studies recruited via the same UK syndrome support group.

2.2. Comparison of prevalence across syndrome groups

Only a few studies utilise a group contrast design. Of the 39 studies, only three compared aggression prevalence figures across groups. These studies are listed in Table 2, and provide insight into which syndrome groups may display comparatively more aggression. Both the studies by Sloneem et al. (2011) and Arron et al. (2011) found that aggression was significantly more prevalent in SMS than individuals with mixed aetiological intellectual disabilities (HID).

Table 2
Studies reporting comparisons of prevalence rates of aggression across syndrome groups.

Authors	Syndrome specific differences in the prevalence of aggression
Sarimski (1997a)	FXS > PWS, WS
Sloneem et al. (2011)	SMS > HID
Arron et al. (2011)	AS, SMS > HID = CdCS, CdLS, FXS, PWS

Table 3
The number of papers considered, and the number of papers identified to investigate the form of aggression, and the role of environmental influences for each syndrome group.

Syndrome (number of papers considered)	Number of papers reporting on the form of aggressive behaviour	Number of papers reporting the role of environmental influences
Cri du Chat syndrome (33)	1	0
Smith-Magenis syndrome (53)	1	3
Fragile X syndrome (592)	1	1
Angelman syndrome (105)	1	3
Cornelia de Lange syndrome (45)	1	0
Prader-Willi syndrome (315)	0	2
Williams syndrome (325)	0	0

2.3. Interim summary

The review has highlighted how quantifying the strength of the association between aggression and genetic syndromes is constrained by methodological limitations. However, despite these limitations, the literature implies that certain syndromes groups may show a stronger association with aggression than others. The value of this finding lies in that it provides a first indication of which groups may be at 'higher risk' and thus should be subject to future research. Given the importance of the early identification of individuals at increased risk of developing aggression, future research should move towards a more consistent approach to examining prevalence. More specifically, as well as the increased use of group contrast designs, it is important to develop consensus on the methodology, definition, and time period used when assessing prevalence. Furthermore, it is important to move beyond broad syndrome group descriptions and towards a consideration of age, gender, and genetic-subtype differences within groups.

2.4. Form of aggression and the influence of environmental factors

To identify papers that provided information on the *form* of aggression and/or on the influence of environmental factors in the selected syndromes the initial electronic search was repeated. Any paper that outlined form and/or implicated or discussed the role of environmental factors in the development and/or maintenance of aggression in the syndrome groups was included. Table 3 displays the number of papers that were identified for each syndrome group to investigate these factors.

2.4.1. Form

Additional information regarding form was found for five of the seven syndrome groups reviewed. For AS, Summers et al. (1995) used the Child Behavior Checklist (CBCL; Achenbach & Edelbrock, 1983) and concluded that children were more likely to 'grab at people and things' than they were to 'hit, kick, bite or scratch others'. The Behavior Problems Inventory (BPI; Rojahn, Matson, Lott, Esbensen, & Smalls, 2001) was used in three separate studies to examine the frequency of different forms of aggressive behaviour in FXS, CdLS, and CdCS. Hessl et al. (2008) reported that the most common forms of aggressive behaviour in FXS were hitting others (49%) and kicking others (30%). Rojahn et al. (2012) found that the most frequently endorsed behaviours for CdLS were hitting others (44.4%), and grabbing and pulling others (40.0%); and Collins and Cornish (2002) reported that the most frequent behaviours for CdCS were hitting others (65%) and pulling other's hair (65%). For SMS, Sloneem et al. (2011) used The Checklist for Challenging Behaviour (CCB; Harris, Humphreys, & Thomson, 1994) and found that the most prevalent forms of aggression were hitting and grabbing (>80% of participants) as well as biting, kicking, and pinching (>50% of participants).

2.4.2. Summary and considerations

The findings of these papers appear to indicate that for FXS, CdLS, CdCS, and SMS, 'hitting others' is a shared common form of aggression, but that these behaviours may be less common in individuals with AS. However, drawing conclusions regarding the form of aggression within syndromes, and making comparisons between syndromes is difficult given the very small number of papers in this area. Furthermore, many of the methodological concerns discussed previously remain. It is clear from this review that further studies, particularly those utilising a group comparison design, are required. In addition to the methodological considerations discussed previously in this review, future work outlining the form of aggressive behaviour in genetic syndromes should consider that the use of standardised measures, such as those used above, may result in idiosyncratic forms of aggression being missed.

2.4.3. Environmental influences

Despite evidence suggesting that the most successful interventions for challenging behaviour seek to define the cause or function of the behaviour before intervening (Harvey et al., 2009), papers examining the role of environmental factors in the development and/or maintenance of aggression were found for four of the syndrome groups only. An overview of these papers is presented in Table 4.

Table 4
Environmental influences on aggression in genetic syndromes.

	Authors	*N*	Study aim	Method	Main findings
AS					
AS	Strachan et al. (2009)	12	To examine the hypothesis that aggression in children with AS would occur at a higher rate when social contact is withheld due to an increased propensity to seek out, and interact with others	Experimental functional analysis	Aggression was shown by 10 children; 1 child showed aggression maintained by attention, 3 children showed aggression during social interaction, and 2 children showed escape motivated aggression. The pattern of results, particularly aggression during social interaction, did not confirm the initial hypothesis. However, the authors argued that evidence of positive affect alongside aggression during the social interaction condition might suggest that aggression serves to both maintain *and* initiate social contact in AS
AS	Didden et al. (2009)	79	To examine the function of communicative behaviours in 79 individuals with AS	Indirect functional analysis methodology: The Inventory of Potential Communicative Acts Questionnaire (IPCA; Sigafoos et al., 2000)	Findings indicated that aggression functioned most commonly to 'reject/protest' (28%) and to 'comment' (33%). Based on their findings, the authors suggested that aggression in AS may be maintained by negative reinforcement.
AS	Radstaake et al. (2012)	4	To examine the function of challenging behaviour in 4 children with AS and assess the effects of functional communication training	Experimental functional analysis	All 4 children exhibited aggressive behaviour. Although the specific function varied for each child, the frequency of this behaviour was influenced by environmental variables such as level of attention, access to tangibles, and demand
FXS					
FXS	Langthorne and McGill (2012)	34	To examine between-syndrome differences in the function of problem behaviour for FXS and SMS	Indirect functional analysis methodology: The Questions about Behavioral Function Scale (QABF; Matson & Vollmer, 1995)	Findings for FXS showed 6.2% displayed attention-maintained aggression, 46.9% tangible maintained, 59.4% escape maintained, 21.9% discomfort related, and 3.2% self stimulatory. Together with findings for the function of self-injurious behaviour and destructive behaviour, the authors concluded that children with FXS may be more likely to display 'escape' or 'tangible maintained' problem behaviours than 'attention maintained' behaviours
SMS					
SMS	Taylor and Oliver (2008)	5	To examine the association between problem behaviour in SMS and environmental events indicative of social reinforcement processes	Sequential analysis of observational data	All participants exhibited aggressive/disruptive behaviour. Results indicated that for 2 (out of 4 participants for whom analysis was possible) aggressive/disruptive was significantly associated with low levels of adult attention. Together with results for self-injury the authors concluded that preference for adult contact and challenging behaviour in SMS may illustrate a potential phenotype–environment interaction
SMS	Sloneem et al. (2011)	28	To investigate the prevalence and phenomenology of aggressive behaviour in SMS. Also, as previous studies have suggested that people with SMS may have a propensity to seek adult contact, to examine the association of aggression with environmental events	Indirect functional analysis methodology: The Questions about Behavioral Function Scale (QABF; Matson & Vollmer, 1995)	Findings indicated that, for the whole group, the 'attention' subscale of the QABF yielded the highest mean score for physical aggression. The authors consequently argued that it is likely that operant factors play a role in the development of aggression in SMS. Furthermore, the authors discuss that results of 'attention maintained' aggression are consistent with reports that people with SMS have a preference for adult contact. Findings replicate and extend the study by Taylor and Oliver (2008)

Table 4 (*Continued*)

	Authors	*N*	Study aim	Method	Main findings
SMS	Langthorne and McGill (2012)	25	To examine between-syndrome differences in the function of problem behaviour for FXS and SMS	Indirect functional analysis methodology: The Questions about Behavioural Function Scale (QABF; Matson & Vollmer, 1995)	Results indicated that 62.5% of participants with SMS met criteria for attention-maintained aggression and 70.8% also met criteria for physical-discomfort related aggression. Taken together with findings for the function of self-injurious behaviour and destructive behaviour, the authors concluded that problem behaviours in SMS may serve multiple functions
PWS					
PWS	Woodcock et al. (2009a)	46	To investigate the context of specific profiles of repetitive behaviour associated with PWS and FXS	Semi-structured interviews that focussed on behavioural and environmental contexts	Findings indicated that anger/aggression was seen in 71.1% of individuals with PWS following changes to routines or expectations. The authors argued that a decrease in predictability is aversive to children with PWS and thus may trigger aggressive outbursts
PWS	Woodcock et al. (2009b)	28	To extend previous findings (Woodcock et al., 2009a) by examining the relationship between preference for predictability and executive dysfunction in individuals with PWS and FXS	Cognitive assessments of executive functioning and informant questionnaires	Findings indicated an attention switching deficit. Furthermore, switch cost was found to be associated with scores on questionnaire items relating to preference for routine and predictability. Together with previous findings the authors hypothesised that changes to routine may trigger aggressive outbursts in PWS because a decrease in predictability is aversive due to an underlying deficit in attention switching

2.4.4. Summary and considerations

Surprisingly few papers were found that examined the influence of environmental factors on aggression. However, findings from the papers listed in Table 4 all implicate the importance of environmental factors, and suggest that aggression may be mediated by different environmental influences for different groups. Furthermore, some findings point towards an interaction between phenotypic characteristics and environmental influences. For example, it was found that a desire for adult attention in SMS and AS (Sloneem et al., 2011; Strachan et al., 2009; Taylor & Oliver, 2008), and a preference for predictability in PWS (Woodcock, Oliver, & Humphreys, 2009a, 2009b) may influence the occurrence of aggressive behaviour in these groups.

Despite these findings, a number of methodological limitations relating to the assessment of behaviour need to be taken into consideration before drawing conclusions. Different methods of analysis were used in the studies listed above. Some of the studies examined naturally occurring antecedents and consequences through observational data, rating scales, or interviews, whereas others used experimental methods of functional analysis. These different methods give rise to different constraints.

One of the main advantages of experimental functional analysis over other methods is that by experimentally manipulating the antecedents or consequences of behaviours, greater control over environmental variables is possible. Conventional experimental functional analysis, as used by Strachan et al. (2009) and Radstaake, Didden, Oliver, Allen, and Curfs (2012) in their studies with AS, test the effects of a specific set of establishing operations: levels of social attention, demand, and access to tangibles. However, it is possible that these methods may not provide the scope to identify idiosyncratic or unusual functions. The same difficulty regarding the identification of idiosyncratic or unusual functions arises in the studies by Sloneem et al. (2011) and Langthorne and McGill (2012) who use the Questions about Behavioral Function Scale (QABF; Matson & Vollmer, 1995) to examine behavioural function indirectly. The QABF is restricted to five predetermined functions and therefore, it is possible that parental responses may not map onto the contingencies that influence the person's behaviour. Therefore, although these studies provide an insight into the behavioural functions of aggression in these groups, a finer grained analysis may be beneficial. However, the QABF does have the advantage of sampling across a longer time period than would be the case for experimental methods.

3. Discussion

The first aim of this review was to examine the extent to which aggression was associated with genetic syndromes. As expected, the prevalence rates for aggression in DS were consistently low (8.6%. 6.0%, 12.0%, 4.4%, and 3.7%). Low prevalence rates were also reported consistently for WS (6.7%, 8.6%, and 15.0%). Moreover, when compared against the prevalence rates for aggression in ID reported in the review by Davies and Oliver (2013), it would appear that these groups show less

aggression than expected, a phenotypic characteristic that warrants comment and explanation. In contrast, the prevalence rates reported for the other syndrome groups included some very high estimates. The highest estimate of 88% was reported for CdCS, but the SMS, FXS, AS, CdLS, and PWS groups all had high end estimates above 70% suggesting that aggression features prominently in these groups. Although limitations relating to methodological constraints are outlined, the value of these findings is that they provide a first insight into which groups may present as 'higher risk' and thus should be subject to future research.

The prevalence of known correlates of aggression within these syndromes is of interest. Correlates of aggression include characteristics of ASD, reduced communication skills, impulsivity, over-activity, and repetitive behaviour (Arron et al., 2011; Dominick et al., 2007; Kanne & Mazurek, 2011; McClintock et al., 2003). Typically, these behaviours are not frequently noted in DS and WS (Dykens, 2003, 2007; Udwin & Yule, 1991), but have been described in the other groups (Arron et al., 2011; Clarke & Marston, 2000; Clarke & Boer, 1998; Collins & Cornish, 2002; Dykens & Cassidy, 1995; Dykens & Kasari, 1997; Einfeld et al., 1999; Finucane et al., 1994; Hagerman, 2002; Hatton et al., 2002; Moss et al., 2011; Sullivan et al., 2006; Summers & Feldman, 1999; Van Buggenhout et al., 2000). Consequently, it might be that these groups share common characteristics that increase their risk of developing aggression.

The review drew attention to the impact that methodological differences between studies may have had on the variation of prevalence rates. Many of the studies utilised different assessment methodologies which in turn, resulted in a number of different definitions and time periods being used to derive estimates. One way to overcome some of these difficulties, and allow for comparisons to be drawn between syndrome groups, is through the implementation of group contrast designs. However, the current review highlighted that, at present, very few studies that document aggression in genetic syndromes have utilised such a design. Consequently, the results of this review demonstrate that future research that assesses the prevalence of aggression in genetic syndromes should be conducted in a more consistent way with group contrast designs. This is particularly important given that although estimates did vary widely, high rates of aggression were reported for CdCS, SMS, FXS, AS, CdLS, and PWS. Accurate identification of individuals at increased risk of developing aggressive behaviours requires that these prevalence rates, and hence relative risk, are established more accurately.

The second aim was to further delineate aggression by examining the form of aggression in the groups, and the influence of environmental factors. Examination of the literature indicated that very few studies had moved beyond broad prevalence estimates of aggression to examine the behaviour in more detail. For the studies that had, drawing strong conclusions was made difficult by a number of methodological limitations, and the lack of comparable studies that replicated results.

One overarching difficulty that was demonstrated both in studies exploring prevalence, and those exploring form and environmental influences, was the lack of emphasis many studies placed on examining gender, genetic-subtype, or age differences. Studies have demonstrated that, in at least some groups, age, gender, and subtype factors are important to consider when examining aggression (Arron et al., 2011; Bailey et al., 2008; Bottani et al., 1994; Hartley et al., 2005; Loesch et al., 2004). Accurate identification of individuals at increased risk of developing aggressive behaviours requires that any potential differences relating to age, gender, or genetic-subtype are explored further.

Although methodological limitations clearly impact on the strength of the conclusions that can be drawn from the existing literature in this area, this review has highlighted a number of important points. A substantial research literature highlights the importance of environmental factors and operant learning in the development, and maintenance of challenging behaviours such as aggression (e.g. Marcus, Vollmer, Swanson, Roane, and Ringdahl, 2001). However, there is also evidence that biological and genetic factors play an important role (e.g. Arron et al., 2011; Langthorne & McGill, 2012; May et al., 2009). The current review points towards the necessity to integrate these two models. More specifically, biological models and genetic factors alone are insufficient to account for aggression in genetic syndromes as this would predict no within syndrome variability and no effect of operant processes on behaviour. Yet, methodological limitations aside, the current review has highlighted within syndrome variability and has also outlined a number of papers demonstrating the effect of operant processes on aggression in genetic syndromes (e.g. Langthorne & McGill, 2012; Sloneem et al., 2011; Strachan et al., 2009). Similarly, environmental factors and operant theory alone are insufficient to account for aggression in genetic syndromes as this would predict that prevalence rates would be equal across groups (because environmental influences are consistent across groups). Yet, prevalence estimates and group comparison designs suggest that some syndrome groups may display comparatively more aggression than others (e.g. Arron et al., 2011; Sarimski, 1997a, 1997b; Sloneem et al., 2011).

This review points towards the importance of phenotype–environment interactions in the development of aggression in genetic syndromes. More specifically, the review reports papers that begin to describe phenotype-specific characteristics which lead to an increased motivation or predisposition, which is then sensitive to environmental factors and operant processes. For example, in the study by Strachan et al. (2009) examining aggression in AS, it was suggested that a genetic predisposition to seek out and interact with adults, may underpin aggression if attention is presented contingent on this behaviour. Similarly, the studies examining the function of aggression in SMS, suggest that aggression may function to elicit attention as a result of an accentuated preference for adult contact (Langthorne & McGill, 2012; Sloneem et al., 2011; Taylor & Oliver, 2008). Furthermore, the review has highlighted papers that begin to describe syndrome-specific cognitive characteristics which may lead to a predisposition to find particular situations aversive. For example, the studies examining aggression in PWS suggest that changes to routine may trigger aggressive outbursts because a decrease in predictability is aversive. It is hypothesised that such difficulties are underpinned by an underlying executive function deficit in task switching/mental flexibility (Woodcock et al., 2009a, 2009b). Overall, these papers emphasise the importance of building

causal models of aggression that take into consideration the interaction between person characteristics and environmental factors (see Oliver et al., 2013, for further discussion)

With phenotype–environment interactions in mind, a comparison of the form of aggression across groups warrants further attention. Closer examination of the form of aggression may provide insight into the underlying predisposition or motivation for the behaviour. Given findings from papers examining function, it is interesting that the most common forms of aggression in FXS were 'hitting and kicking others' whereas, in AS the most common forms were 'grabbing and pulling'. More specifically, papers examining function demonstrated that children with FXS were more likely to display 'escape' or 'tangible maintained' aggression (Langthorne & McGill, 2012) whereas for AS, it has been hypothesised that aggression may function to maintain social contact (Strachan et al., 2009). It could be considered that 'grabbing and pulling' would be more effective to prolong social contact whereas 'hitting and kicking' would be more effective to 'escape'. Although it is important to stress that findings of the current review are limited due to the extremely small number of studies conducted that outline both form and function, the findings highlight the importance of looking beyond broad behavioural phenomenology and towards a more detailed study of behavioural characteristics.

Such findings relating to the role of phenotype–environment interactions have important clinical implications. Intervention strategies to reduce aggression in individuals with genetic syndromes may be enhanced by shifting focus away from the behaviour, and towards the underlying motivation or predisposition that is sensitive to operant reinforcement. For instance, for PWS, cognitive training, or interventions that make change less unexpected, may be beneficial. Furthermore, methodologies used in the assessment of aggression should incorporate designs that not only determine environmental influences but also investigate whether a specific motivation of predisposition is driving the behaviour. For example, an additional assessment of social motivation for individuals with AS may provide important additional information to inform intervention.

An interesting observation that arose from this review was the striking lack of information regarding aggression in ID and genetic syndromes when compared to the parallel literature documenting self-injurious behaviour. In the self-injury literature there are numerous reviews, papers outlining the early development of self-injury, predicted persistence, assessment and intervention, and models (e.g. Carr, 1977; Deb, 1998; Emerson et al., 2001; Emerson, 1991; King, 1993; Oliver, Hall & Murphy, 2005; Oliver, 1995; Rojahn, Schroader & Hoch, 2007). Furthermore, it has been noted that aggression *is* present in other syndromes such as Rett Syndrome (RS) (Naidu et al., 1990) and Lesch-Nyhan syndrome (LNS) (Schretlen et al., 2005) but studies have yet to delineate this aggression or document the extent to which it is associated with these groups. One explanation for this disparity is that aggression is overlooked in some syndromes because other, more prominent features take precedence. For LNS, this might be the extremely high rate of very severe self-injury, or in RS, the characteristic hand stereotypies. However, this would not explain why generally, there is a smaller body of research outlining aggression in ID and genetic syndromes. Another explanation could be that aggression might be perceived as a more 'understandable' or typical behaviour than self-injury and thus has not prompted the same level of interest or enquiry. For example, it is perhaps easier to see the potential reasons for why a person with an ID might be aggressive, than to see the reasons for self-injury. Although a body of research has investigated causal attributions about challenging behaviour in people with ID (e.g. Hastings, Reed, & Watts, 1997), it would be informative to examine whether people's attributions or understanding of challenging behaviours differ for the different types of behaviours.

In summary, this paper has highlighted important directions for future research. Accurate identification of individuals at risk of developing aggression requires that research is conducted in a more consistent and robust way, comparing directly across groups. The impact of age, gender, and genetic-subtype differences on aggression should also be explored. Future work on the assessment and intervention of aggression, should consider the importance of phenotype–environment interactions and finally, attention should be paid to the possible reasons why aggression has received comparatively less attention to the examination of self-injurious behaviour in genetic syndromes.

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