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Self-injurious behaviour in Cornelia de Lange
syndrome.: 1. Prevalence and phenomenology.

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Abstract

Background. Self-injurious behaviour is frequently identified as part of the behavioural phenotype of Cornelia de Lange syndrome (CdLS). We conducted a case-control study of the prevalence and phenomenology of self-injurious behaviour (SIB) in CdLS.

Methods. 54 participants with CdLS were compared to 46 individuals who were comparable on key variables including age, degree of intellectual disability and wheelchair use, using questionnaire and observational measures.

Results. Clinically significant self-injury was not more prevalent in the CdLS group (55.6%), nor was it different in presentation from that seen in the comparison group. Hyperactivity, stereotyped and compulsive behaviours predicted clinically significant self-injury in all participants. Hand directed, mild self-injury was more prevalent in CdLS.

Conclusions. The results show that clinically significant self-injury may not be part of the behavioural phenotype of CdLS but a specific body target for proto-SIB is more common.

Keywords: Self-injurious behaviour, Cornelia de Lange syndrome, behavioural phenotype, repetitive behaviour, stereotyped behaviour, compulsive behaviour

Introduction

Cornelia de Lange syndrome (CdLS) is a genetic disorder associated with a chromosomal disorder on the short arm of chromosome five in 50% of cases (Krantz, *et al.*, 2004; Tonkin, Wang, Lisgo, Baumshad & Strachan, 2004). Additional mutations on the SMC3 gene on chromosome 10 (Deardorff *et al.*, 2007) and X linked SMC1 gene (Musio *et al.*, 2006) are reported to account for 5% of cases. The physical phenotype has been described extensively and includes characteristic facial features (confluent eyebrows, long eyelashes, long philtrum, a thin upper lip and a down turned mouth) that are influential in clinical diagnosis (e.g. Hawley, Jackson, & Kurnit, 1985; Ireland, Donnai & Burn, 1993; Jackson, Kline, Barr & Koch, 1993; Ptacek, Opitz, Smith, 1963). Limb abnormalities are frequently present and range from mild anomalies (i.e. small hands and feet, short digits, proximally placed thumbs, clinodactyly of fifth fingers and webbing of toes) to severe arm defects such as oligodactyly (the absence of one or more fingers) and phocomelia (the absence of the upper portion of one or both arms). Other characteristics include: small stature (Ireland *et al.*, 1993), excessive hair growth (on the forehead, upper lip, nape of the neck and on the back), gastrointestinal problems (Berg *et al.*, 2007; Hall *et al.*, 2008; Luzzani, Macchini, Valade, Milani & Selicorni, 2003) heart defects (Jackson *et al.*, 1993), eye disorders (Levin & Shin, 1995) and hearing loss (Sataloff, Spiegel, Hawshaw, Epstein & Jackson, 1990).

Previous research has described the behavioural and cognitive characteristics of people with CdLS although case control studies are lacking. Degree of intellectual disability ranges from mild to profound with moderate to severe intellectual disability the norm (Berney, Ireland & Burn, 1999, Oliver *et al.*, 2008). Speech and language deficits have been noted, especially compromised expressive language (Goodban, 1993; Hawley *et al.*, 1985; Kline *et al.*, 1993; Oliver *et al.*, 2008). An autistic like syndrome has been reported in many people with the disorder (Berney *et al.*, 1999; Basile *et al.*, 2007; Bhuyian *et al.*, 2006; Collis *et al.*, 2008) and an elevated prevalence of autistic like disorder has been confirmed in a case control study (Oliver *et al.*, 2008) and a syndrome contrast study (Moss *et al.*, 2008). More specific behaviours such as back arching, and repetitive behaviours (i.e. hand posturing and regard, vestibular movements, body twirling and body turning) have also been

reported (Johnson, *et al.*, 1976). Back arching has been suggested to be related to gastroesophageal reflux, a common physical disorder in the syndrome (Jackson *et al.*, 1993; Berg *et al.*, 2007). Self-injurious behaviour has frequently been reported in people with CdLS (Beck, 1987; Berney *et al.*, 1999; Gualtieri, 1990; Hawley, *et al.*, 1985; Johnson *et al.*, 1976, Hyman *et al.*, 2002).

The first reports of self-injurious behaviour in Cornelia de Lange syndrome were published in 1971 (Bryson, Sakati, Nyhan & Fish, 1971; Shear, Nyhan, Kirman & Stern, 1971). Soon after, Nyhan (1972) suggested that the association between the syndrome and behaviour was so strong that self-injury formed part of the behavioural phenotype. Since this time a number of authors have suggested that the prevalence of self-injury in CdLS is high in comparison to populations of people with mixed aetiological intellectual disability. Whilst the prevalence of self-injurious behaviour in the latter group generally falls below 25% (Oliver, 1993; McClintock, Hall & Oliver, 2003), the majority of studies detailing the prevalence in CdLS report a figure in excess of 50% (Beck, 1987; Berney *et al.*, 1999; Gualtieri, 1990; Hawley, *et al.*, 1985; Hyman, Oliver & Hall, 2002; Johnson, Ekman, Friesen, Nyhan & Shear, 1976). The increased prevalence of self-injury in CdLS has resulted in the behaviour being seen as a distinctive and invariant feature of the syndrome. However, despite this high prevalence little research has been undertaken to delineate the phenomenology and predictors of self-injury and no published studies have employed comparison groups.

In terms of the underlying aetiology of self-injury in CdLS, it is unclear whether causes are syndrome specific or are the same as those seen in people with intellectual disabilities of mixed aetiology. Self-injury has been reported to be associated with gastro-intestinal reflux (Luzzani, Macchini, Valade, Milani & Selicorni, 2003) and operant processes (Arron *et al.*, 2006; Moss *et al.*, 2005). As noted above, CdLS is associated with many risk markers for self-injurious behaviour i.e. more severe intellectual disability (Beck, 1987; Hawley *et al.*, 1985; Kline *et al.*, 1993), sleep problems (Gualtieri, 1990), expressive communication deficits (Beck, 1987; Berney, *et al.*, 1999; Goodban, 1993; Hawley *et al.*, 1985; Sarimski, 2002), potential insensitivity to pain (Kline *et al.*, 2001), compulsive behaviours (Bryson *et al.*, 1971; Hyman *et al.*, 2001; Shear *et al.*, 1971; Oliver *et al.*, 2008; Moss *et al.*, 2009) and

autistic characteristics (Berney *et al.*, 1999; Johnson *et al.*, 1976; Oliver *et al.*, 2008). A meta-analytic evaluation of prevalence studies of self-injury has shown that factors such as these are predictive of relatively high prevalence figures for self-injury (McClintock *et al.*, 2003).

In addition to increased prevalence of self-injury, individuals with some genetic syndromes are more likely to display specific *forms* of the behaviour than individuals without such diagnoses. These specific expressions of behaviour have contributed to the notion that certain topographies of self-injury are part of the behavioural phenotype of particular syndrome groups. Skin picking is commonly reported in Prader-Willi syndrome (Dykens, Hodapp, Walsh & Nash, 1992; Dykens & Kasari, 1997; Greenswag, 1987; Whitman & Accardo, 1987), whilst nail removal (rarely mentioned elsewhere) is reported relatively frequently in descriptions of people with Smith-Magenis syndrome (Lockwood *et al.*, 1988; Smith *et al.*, 1986). As well as specific forms of self-injury, people with different syndromes may also be more prone to targeting specific *locations* of the body depending on their diagnoses. For instance, people with Lesch-Nyhan syndrome are reported to injure their lips and fingertips (Anderson & Ernst, 1994, Hall *et al.*, 2001), whilst those with Rett syndrome direct their injury towards their hands (Coleman, 1988). Despite initial reports focusing on lip-biting in CdLS (Shear *et al.*, 1971) and later reports that that finger-biting is common (Beck, 1987) recent research has not supported the idea that the syndrome is associated with either particular forms of SIB or specific body site locations. However, most reports have used standardised questionnaires that may omit rare forms of self-injury and, as yet, no studies have been carried out to examine the distinctiveness of the expression of self-injury in CdLS relative to those without the syndrome.

Evaluation of behaviours such as self-injury in behaviour phenotype research presents problems of definition. Identification of behaviour of clinical significance is clearly of importance for service provision and intervention planning. However, more subtle behaviours that are potentially injurious but not immediately evident are of interest both because of their potential for transformation into more severe problems (Oliver, 1993; Guess and Carr, 1993) and in their own right as potential facets of a behavioural phenotype. Thus, appraisal of prevalence of behaviour should be conducted at levels

of clinical significance and using direct observation of operationally defined behaviours.

In this study we examine the extent to which self-injury is part of the behavioural phenotype of CdLS. Given the available data on risk markers for self-injury and the acknowledged importance of matching groups in behavioural phenotype studies (Hodapp and Dykens, 2001) we explore the association between syndrome and behaviour using a comparison group to control for the level of intellectual disability, mobility, age and gender. We also explore and compare the influence of predictive characteristics on the manifestation of self-injury in the two groups, i.e. whether risk markers predict self-injury in CdLS and comparison group similarly. The strategy is to build a model to predict the manifestation of self-injury in all participants and determine whether a diagnosis of CdLS significantly adds to the predictive properties of the model. Finally, we compare and contrast the phenomenology of SIB in CdLS and the Comparison group and determine whether the types of self-injury displayed by people with CdLS are evident in people without the syndrome.

Method

Participants and recruitment

Fifty-four people with CdLS and 46 people with intellectual disabilities of mixed aetiologies took part in the study. Data from all participants were used to determine the prevalence of self-injury and derive a model to predict the behaviour. The Challenging Behaviour Interview (Oliver, McClintock, Hall, Smith, Dagnan, *et al.*, 2003) was used to identify the subset of participants who manifested clinically significant self-injurious behaviour and observations from 29 participants with CdLS and from 17 people without the syndrome were analysed to examine and compare the phenomenology of self-injury in the two groups.

Participants with CdLS were predominantly recruited via the CdLS Parent Foundation group (UK and Ireland). A proportion of participants had been involved in a previous survey study (Hyman, Oliver & Hall, 2002) and were initially recruited via the parent group, these individuals were contacted directly (N = 75). Information was also sent

via the Foundation to all remaining members (N = 112). Three additional participants were recruited by professionals in the local area. Participants were selected if they were aged over two years and lived within 100 miles of five research bases in the UK and Ireland.

This research was undertaken prior to the identification of the genetic marker for Cornelia de Lange syndrome. Consequently, carers of participants in the CdLS group provided information relating to diagnoses made by clinical geneticists, paediatricians and physicians. The diagnosis of CdLS was queried for a small number of participants due to the absence of specific facial characteristics typically seen in individuals with CdLS (Ireland, Donnai & Burn 1993). For this subset of 13 people, a second opinion was sought from a clinical geneticist who is the Medical Director of the CdLS Foundation in the USA. Her opinion led to five participants being excluded from the study.

A comparison group comprising people matched to individuals with CdLS in terms of age, gender, mobility and level of ability (with mobility and level of ability assessed by the Wessex, Kushlick et al., 1973) was recruited in one of two ways. Firstly, the teachers and key workers of participants with CdLS identified up to two individuals in their school or center who were similar in terms of the comparison parameters to the index participant. This strategy yielded five participants. Secondly, project information and demographic questionnaires were distributed to every pupil or client within each eight schools and four Social Education Centres (N = 876). Consent forms and questionnaires were returned by 153 carers (17.5%), of which 41 matched an individual in the CdLS group and were selected for the study. Table one displays participant characteristics. Detailed comparisons of the groups on variables described in table 1 are reported in Oliver et al., (2008)

+++++ Insert Table 1 here +++++

Measures

Primary caregivers and teachers or key workers completed questionnaires and acted as informants for standardised interviews.

Demographic information. A brief questionnaire was used to ascertain diagnostic and demographic information about participants and informants.

Sensitivity to pain. Information relating to sensitivity to pain was obtained from a question with a seven-point Likert scale response rating the degree to which the participant was sensitive to painful stimuli. Inter-rater reliability was collected for this question on fifteen participants and the intra-class correlation coefficient was satisfactory at .87.

Sleep disturbances. Sleep difficulties were assessed with the Infant Sleep Questionnaire (ISQ) (Morrell, 1999). The ISQ is a ten-item questionnaire divided into sections concerning ‘going to bed/sleep’, ‘waking at night’ and ‘sleeping in the carer’s bed’. Carers rate how frequently problems occur, how long settling takes at night and how long these problems have been occurring. An overall sleep score ranging from 0 – 38 may be obtained by summing six of the questions.

Autism. The Gilliam Autism Rating Scale (GARS) Gilliam (1995) is a fifty-six item behavioural checklist used for the purpose of screening for autism. It comprises four subscales: stereotyped behaviours, communication, social interaction and developmental disturbances. Items are rated on four-point scales according to frequency (0 - never observed to 3 - frequently observed). Raw scores are summed for each subscale and converted into standard scores from which an autism quotient may be determined. The quotient is broken down into seven categories, ranging from a “Very Low” to a “Very High” probability of autism. A score of 90 or above indicates that the child is “probably autistic.” One item on the stereotyped behaviour subscale may be classified as self-injurious. Consequently, for the analyses in which autism was used to predict self-injury, the item was removed and the total subscale score pro-rated.

Challenging and aberrant behaviours. The Aberrant Behavior Checklist – community version (ABC-C) (Aman, Singh, Stewart & Field, 1985a; Marshburn and Aman, 1994) is a 58 item questionnaire assessing the degree to which individuals with intellectual disabilities display behaviour disorder. Items are rated on four-point

Likert scales ('no problem' to a 'severe problem') in five categories: 1) Irritability, agitation crying, 2) Lethargy, social withdrawal 3) Stereotypic behavior 4) Hyperactivity and non-compliance and 5) Inappropriate speech. The questionnaire was used to obtain information specifically on hyperactivity and stereotypies only (subscales three and four).

Compulsive behaviour – The Compulsive Behavior Checklist (CBC) (Geyde, 1992) lists twenty-five topographies of compulsive behaviours which are grouped into five categories: ordering, completeness/incompleteness, cleaning/tidiness, checking/ touching and grooming compulsions.

Challenging Behaviour The Challenging Behaviour Interview (CBI) (Oliver *et al.*, 2003) is a two-part interview used to assess the prevalence and severity of challenging behaviours displayed by people with intellectual disabilities. In part one, five forms of challenging behaviours (including self-injurious behaviour) are presented. Self-injury is defined as 'Non-accidental behaviours which produce temporary marks or reddening of the skin or cause bruising, bleeding or other temporary or permanent tissue damage [Examples - Self-biting, head banging, head punching or slapping, removing hair, self scratching, body hitting, eye poking or pressing]'. Informants state whether each of the behaviours have been displayed in the past month. In part two, fourteen questions are asked to determine the severity of the behaviour for each behaviour identified. Each question has a four or five-point Likert scale, lower scores reflecting less severe behaviour. The scores for each of these questions are aggregated to provide an overall severity score for each behaviour. Psychometric properties of the interview have been calculated, i.e. test-retest reliability, inter-rater agreement, concurrent and content validity were generally reported to be good. (Oliver *et al.* 2003).

Adaptive Behavior – The Vineland Adaptive Behavior Scales – Survey Form (Sparrow, Balla & Chicchetti, 1984) was used to assess each participant's personal and social adaptive behaviour levels and level of intellectual disability. The VABS-SF is administered as a semi-structured interview, which is suitable for individuals with and without intellectual disabilities. The interview consists of 261 items divided into four domains: communication, daily living skills, socialization and motor skills.

Observational Data Collection –Natural observations were undertaken in the participant’s normal day care environment. Operational definitions of self-injurious behaviours were developed following informal observations, preliminary analysis of videotapes and a literature search. Each topography of self-injury was coded separately to allow fine-grained analysis of phenomenology to be undertaken. These observational definitions differed from those used to identify clinically significant SIB (as defined by the CBI) and could encompass very mild forms of SIB. Operational definitions of participant’s behaviours are presented in table 2.

+++++++ Insert Table 2 here ++++++

Following coding, *all* individual topographies of SIB were combined to form an overall category of ‘global self-injurious behaviour’. Categories of self-injury were additionally clustered by form. These included: ‘picking self’ (which comprised body picking, face picking, hand picking, head picking and neck picking), ‘poking self’ (body poking, ear poking etc., eye poke and face poke), ‘striking self’ (body hit, face hit and head hit), ‘biting self’ (hand bite and lip bite) and ‘body to object injury’ (body bang, body throw, elbow flick and head bang). Self injurious categories were also collapsed by location. These comprised: ‘body directed’ (body bang, body hit, body pick, body poke, body throw), ‘face directed’ (face hit, face pick and face poke), ‘sense organ directed’ (ear poke and eye poke), ‘head directed’ (head bang, head hit, head pick and neck pick), ‘hand directed’ (hand bite, hand pick and finger insertion), and ‘mouth directed’ (lip bite and mouth flick). Global SIB was defined as the total of all topographies of SIB.

Procedure

Participants were visited in their usual day-care environment. One week prior to the research visit, questionnaires were sent to carers and teachers/key workers. Observations were collected over the course of the day (mean observation time 245.7 minutes, SD 31.9, range 137 minutes to 298 minutes). Activities observed were typical of settings (e.g. meal times, group and individual activities, leisure time). Sony TRV-48E video camera recorders were used and for filming and LCD fold out

screens were used to minimise observer reactivity.

Observational data were transferred onto VHS tapes and were coded by two observers (JS and KA) using Obswin 32 software (version 3.0) (Martin, Oliver and Hall, 2000). Obswin 32, uses real time analysis and enables behaviours to be recorded both as ‘discrete events’ (nominated 1s duration) and ‘durations’ in which onset and offset times are recorded. Inter-observer reliability was calculated for 26.33% of observations. Kappa values were calculated for each behavioural code on a ten-second interval-by-interval basis. Kappa values derived were all ‘good’ or ‘excellent’ (Fleiss, 1981 in Bakeman & Gottman, 1997) (range .67 to 1.00). Two topographies of behaviours (body poking and elbow flicking) were not observed in the inter-observer evaluations.

Results

Independent samples t-tests and χ^2 tests revealed no significant differences between the Comparison and CdLS groups in terms of age, gender, Vineland Adaptive Behavior Scale classification and wheelchair use. The groups are therefore comparable on these variables.

Prevalence of self-injury and other behaviour disorder

Prevalence figures for self-injury and other behaviour disorders manifested by individuals with CdLS and the Comparison groups were determined from data from the Challenging Behaviour Interview and are shown in table 3 together with odds ratios. 55.6% of those diagnosed with CdLS showed self-injury compared to 41.3% of the Comparison Group but this difference is not statistically significant. Similar analyses for other forms of behaviour disorder also revealed no differences between the groups (see Table 3). Secondary analyses considered differences in the prevalence of each form of behaviour disorder reported in table 3 both across and within groups broken down by gender, age (above and below 12 years) and degree of intellectual disability (profound/severe vs. moderate/mild). There were no significant differences either within or between groups in the prevalence of each form of behaviour disorder when broken down by these three variables.

+++++++ Insert table 3 here ++++++

Predicting Self-Injury

Given that no difference in prevalence of self-injury is evident when it is assessed at this level analysis of the variables that predict the presence of self-injury was undertaken across groups. Additionally, group membership was added to the predictor variables to evaluate if prediction was improved when other variables were controlled for. To evaluate which characteristics, including group membership, predicted the presence of self-injury a forced entry binary logistic regression was conducted. Nine independent variables were force entered into the model (age, sensitivity to pain, autism quotient, compulsion score, hyperactivity score, stereotypy score, mobility score, adaptive behaviour score and sleep problem score). A further independent variable 'diagnostic category' (CdLS or Comparison) was force entered into the second block to determine whether a 'diagnostic category' significantly adds to the predictive properties of the existing model. The model correctly classified 76.5% of cases and three variables significantly contributed to the prediction of self-injury: number of compulsions (Wald = 5.30, df (1), $p < .05$, odds ratio = 1.32), hyperactivity score (Wald = 3.93, df (1), $p < .05$, odds ratio = .93) and stereotyped behaviour score (Wald = 8.06, df (1), $p < .01$, odds ratio = 1.29). Diagnostic category did not significantly improve the ability to predict self-injury ($\chi^2 = .185$, df (1), $p = .67$).

To further investigate the variables predictive of self-injury a principle components factor analysis was employed for the behavioural variables significantly predictive of self-injury (hyperactivity, stereotypy, compulsions). The factor analysis extracted a single component with an Eigen value greater than one (Eigen value = 2.24) that accounted for 55.93% of the variance. The factor was tentatively labelled 'behavioural dysregulation' and all factor loadings were acceptable at above .60 (.62, .71, .79 and .82). A final multiple regression analysis was employed in which the 'behavioural dysregulation' factor was entered as the dependent variable. The independent variables simultaneously entered into the equation were; age, pain sensitivity, sleep problems, autism quotient and adaptive behaviour score. Together

these variables accounted for 32% of the variance ($R^2 = .32$, $F(6, 78) = 6.17$, $p < .01$). Two variables, 'wheelchair use' ($B = -.30$, $t = -2.04$, $p = .045$) and 'autism quotient' ($B = .03$, $t = 4.20$, $p < .01$) significantly contributed to the model. Diagnosis of CdLS was force entered into the second block. There was only a small improvement in the proportion of variance accounted for ($R^2 = .35$) and this diagnostic variable did not make a significant contribution to the model ($B = .33$, $t = 1.83$, $p = .07$).

Thus, three variables, arguably underpinned by 'behavioural dysregulation' and predicted by autistic characteristics and mobility contributed to the prediction of the presence of self-injury: the number of compulsions, the hyperactivity score and the stereotyped behaviour score. The diagnosis of CdLS did not improve the prediction of self-injurious behaviour.

Comparison of the severity and phenomenology of self-injurious behaviour.

There was no significant difference between the groups on the mean total Challenging Behaviour Interview severity score for self-injury (mean CdLS score = 15.83, SD 5.88; mean Comparison Group score = 13.11, SD 5.37; $t(47) = -1.63$, $p = .11$). A series of Mann-Whitney U tests revealed no significant differences between the two groups on any item in the CBI.

To examine potential differences between the groups in the observed levels of all self-injurious topographies combined, the proportions in each group showing the behaviour were compared. Statistical analysis revealed a significant difference in the proportions of each group showing self-injurious behaviour (CdLS = 92.5%, Comparison = 76.2%; $\chi^2(1) = 4.93$, $p = .026$). The results of a more fine grained analysis of topography and body site of self-injury, body contact stereotyped behaviours and noncontact stereotyped behaviours was undertaken and the results are shown in Table 4. Within each group of statistical tests, the Alpha level was set at $p < .01$ to minimise type 1 errors. These comparisons show that the groups did not differ in the proportions of participants showing specific topographies of self-injury (although biting approached significance, $p = .02$). However, higher proportions of the CdLS group showed SIB directed toward the hands ($p = .001$), body contact

stereotyped behaviour directed toward both the head ($p < .001$) and body ($p = .001$) and hand posturing ($p < .001$). A secondary analysis of hand directed SIB showed no difference in the proportion of each group showing hand picking (CdLS 52.8%; Comparison 33.3%, $\text{Chi}(1) = 3.61$; $p = .06$) but a higher proportion of CdLS participants showing hand biting (CdLS 54.7%; Comparison 31.0%, $\text{Chi}(1) = 5.37$; $p = .02$).

+++++++ Insert Table 4 here ++++++

Similar additional analyses of other challenging behaviours revealed no differences between the groups for physical aggression, verbal aggression or destruction of property (see table 4). However, a significantly higher proportion of the Comparison group showed combined forms of behaviour than the CdLS group ($p = .006$). Thus, the observational data show the CdLS group evidence a significantly higher prevalence of self-injury, specific forms of self-injury but a significantly lower prevalence of combined forms of challenging behaviour.

Given the significant difference between the groups in hand posturing and the differences in observed presence of SIB and hand directed SIB, the association between hand posturing and these two variables was examined in the CdLS group. Pearson correlations revealed a significant positive correlation between the percentage of time participants with CdLS engaged in hand posturing and the percentage of time engaged in SIB ($r(52) = .43$, $p = .001$) but no correlation with hand directed SIB.

The percentage of time for which each category of self-injury was shown was derived for the CdLS and Comparison groups to examine differences in this parameter of severity. These data are shown in table 5. Mann-Whitney U tests were undertaken to compare the percentage time of forms and targets of self-injury across the groups. Analyses were carried out when more than five participants in each of the CdLS and comparison groups displayed a category of behaviour. Results of these analyses revealed no differences between the groups for location or form.

+++++++ Insert Table 5 here ++++++

The number of individual topographies of self-injury displayed by each participant over the observation period (for greater than or equal to one percent of the time) were summed and compared across groups. In addition, the number of forms (e.g. picking, poking) and number of locations (e.g. face, hand) were totalled. Of the twenty individual topographies of self-injury operationally defined, the median number displayed for 1% of the time or above in both the CdLS and comparison groups was one (Mann-Whitney $U = 245$, $p = .97$). Of the five *forms* of the behaviour, the median number displayed by both the two groups was one (Mann-Whitney $U = 227$, $p = .62$). Finally, of the five self-injurious *locations*, the median number of sites injured for greater or equal to 1% of the time by both the CdLS and comparison groups was also one (Mann-Whitney $U = 222$, $p = .54$). The analyses therefore revealed no significant differences between CdLS and comparison groups.

Discussion

In this study we used observational methods, psychometrically robust measures and a case control design to explore self-injurious behaviour in individuals with Cornelia de Lange syndrome. The design allowed comparison of prevalence, predictors and phenomenology to be made directly between individuals with and without CdLS, whilst controlling for age, degree of intellectual disability, gender and physical disability. Observational data, that it would not be possible to obtain from informant based measures, allowed fine-grained analysis of phenomenology to be undertaken. Such methodology prevents omission of potentially important syndrome specific behaviours.

At 55.6%, the prevalence rate of clinically significant self-injury in people with CdLS was found to be relatively high and comparable to previously reported prevalence figures (see Table 6). The similarity in prevalence to previously reported figures suggests the sample was representative. However, when comparing this figure to a group matched for risk markers for self-injury, no significant difference was found (comparison group SIB prevalence, 41.3%). Thus, self-injury was not found to be significantly more prevalent in individuals with CdLS than those without. In contrast to prior assertions (e.g. Nyhan, 1972, 1994), once other factors have been controlled

for, it is possible to contest that clinically significant SIB is part of the behavioural phenotype of CdLS. The prevalence of SIB identified using the CBI was higher than that identified by observation for both groups. The reason for this is that the observational definitions were very broad in order to encapsulate both SIB and proto-SIB (i.e. all potentially injurious behaviours) given the potential importance of the latter in the early stages of the development of severe SIB..

+++++++ Insert Table 6 here ++++++

The finding that there was no difference between CdLS and comparison groups in terms of prevalence of SIB was explored further by the analysis that considered variables that are commonly related to self-injury in people with intellectual disabilities of mixed aetiology (McClintock et al., 2003). A model was ascertained and when entering ‘diagnosis of CdLS’ as an additional and separate predictor variable, diagnostic status was *not* found to significantly contribute to a model. This result suggests that when taking into account other risk markers for self-injury, a diagnosis of CdLS does not increase the likelihood of self-injury. This supports the above suggestion that clinically significant SIB may *not* be part of the behavioural phenotype of the syndrome. Instead, the syndrome manifests a number of risk markers, characteristics and behaviours, which in turn associate with a relatively high prevalence of SIB.

With reference to age, there was no evidence that prevalence of self-injury in the CdLS or Comparison group increased with age. Additionally, no relationship with degree of intellectual disability was identified between and within groups. This is in contrast to findings of previous prevalence studies of SIB (e.g. Oliver, Murphy & Corbett, 1987; Kebbon & Windahl, 1986) and the results of a meta-analysis (McClintock et al., 2003). These discrepancies may be due to the comparatively small numbers in each sample leading to a lack of statistical power. Gender had no effect on SIB in either of the diagnostic groups in line with the findings of McClintock *et al.* (2003).

The results of this study make a novel contribution to the literature on predictors of self-injury. Three variables significantly contributed to the prediction of self-injury:

stereotypies, compulsions and hyperactivity. From these, a single behavioural factor emerged from a factor analysis, combining self-injury together with these three factors into a single behavioural cluster. Analysis revealed that being diagnosed with CdLS was not a predictive factor in the manifestation of the behavioural disorder and it may be that the underlying behavioural cluster is more common in individuals who display self-injury and is not specific to CdLS. However, two variables *were* significant predictors of this factor; wheelchair use and autism quotient. These findings are not unexpected given that firstly, mobile individuals would be more able to engage in compulsions, or exhibit the behaviours seen as part of a hyperactivity disorder (as measured by the Aberrant Behavior Checklist, Aman *et al.*, 1985a), and secondly, that stereotyped behaviours together with some forms of compulsive behaviours form part of the diagnosis of autism. Further examination of this association would benefit from the use of alternative measures of autism spectrum disorder given some concerns regarding the reliability and validity of the GARS (Lecavalier, 2005).

The finding that three variables, each theoretically associated with behavioural dysregulation, predict the presence of self-injury, supports the idea that self-injury might be influenced by or related to a more general behavioural disorder. This finding provides support for the assertion that a relationship exists between self-injury and stereotyped and compulsive behaviours (King, 1993; Berkson & Tupa, 2000; Guess & Carr, 1991; Rojahn, 1986) and thus proposals that there is a relationship between abnormal repetitive behaviours per se and SIB, (King, 1993, Bodfish & Lewis, 2002; Petty & Oliver, 2005) and that hyperactivity and impulsivity may play a role in the exhibition of the self-injury (Petty & Oliver, 2005; Rojahn, Matson., Naglieri, & Mayville, 2004).

These associations may in part be explained by the theory proposed by Turner (1999) who suggests that individuals who show repetitive behaviour have an impaired capacity to regulate behaviour via the inhibition of ongoing inappropriate behaviour and that the person consequently becomes 'locked' into inappropriate repetitive movements. It is notable that contemporary theories of Attention Deficit and Hyperactivity Disorder also impute disordered behaviour regulation as central to the behavioural manifestation (Barkley, 1997). More recently, Petty and Oliver (2005)

proposed that compromised behaviour regulation, particularly the inability to prevent initiation or subsequent termination of behaviour, are evident in people with severe self-injury and manifest as a preference for imposed restraint or self-restraint (see Oliver, 2003). They state that a plausible hypothesis is that a common cognitive impairment underpins both stereotyped behaviour and impulsivity, and when self-injury comes into the repertoire against this background, restraint is a method of self-control for dysregulated behaviour. The finding that stereotypies, compulsions and hyperactivity predict self injury in the present sample of people with and without CdLS and the previously reported association between self-restraint, compulsive behaviour and self-injury in CdLS (Hyman, Hall and Oliver, 2002) also provides support for these ideas.

Severity and phenomenology of self-injury

Whilst there were no significant differences between the groups in terms of the prevalence or severity of clinically significant self-injury detailed observation revealed some differences in specific behaviours that were potentially injurious. Mild or proto-injurious behaviours directed towards the hands, body and head were noted with a secondary analysis identifying hand biting as more common. This latter finding is of interest when combined with the observation that hand posturing is more common in CdLS. Kline (2001) has suggested that peripheral sensory neuropathy might be evident in CdLS given the gene expression in the upper limbs. It is conceivable that the low level self-injury directed toward the hands is related to a peripheral sensory neuropathy. This possibility is given additional support from the noted association between SIB and hand posturing identified in this study. Hand posturing might be a response to a disorder of proprioception or paresthesia that accompanies peripheral sensory neuropathy. Alternatively the association between hand posturing and self-injury might be accounted for by a third, as yet unknown, variable. For observational data indicative of severity when examining the differences between CdLS and Comparison groups no differences were found in the *number* of topographies or the percentage time or frequency of the behaviours observed between the two groups i.e. the CdLS group did appear to show consistently higher rates (frequency) of behaviours than comparison individuals.

In summary, data from the present study demonstrate that once risk markers for the behaviour are controlled, clinically significant self-injury is not more prevalent in CdLS than in matched individuals without the syndrome and a diagnosis of CdLS does not contribute to the ability to predict the presence of SIB when other risk markers are controlled for. Across groups self-injury is associated with a number of other behavioural disorders, i.e. hyperactivity, compulsions and stereotypies. The reason for this clustering of these behaviours warrants further investigation. At observation some forms of potentially injurious behaviours are more common in CdLS but other forms of problem behaviour are significantly less common, thus demonstrating that these differing forms of behaviour are dissociated in the syndrome.

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Table 1. Characteristics of CdLS and Comparison group Participants

		CdLS (n = 54)	Comparison Group (n=46)
Age	Mean (years) (SD)	13.9 (9.0)	13.7 (8.0)
Males		25 (46%)	23 (50%)
Vineland Adaptive Behavior Scale classification	Profound	27 (50%)	21 (46%)
	Severe	13 (24%)	14 (30%)
	Moderate	8 (15%)	7 (15%)
	Mild	6 (11%)	4 (9%)
Vineland Adaptive Behavior Scale Daily Living Skills domain age equivalent score (in months)	Mean (SD)	32.91 (22.48)	33.02 (22.25)
Wheelchair use	Never	30 (56%)	28 (61%)
	Sometimes	18 (33%)	13 (28%)
	Always	6 (11%)	5 (11%)
Aberrant Behavior Checklist subscale mean scores	Stereotyped behavior	4.23 (5.27)	3.20 (4.43)
	Hyperactivity	13.02 (12.68)	11.10 (11.64)
Gilliam Autism rating scale autism quotient	Mean (SD)	92.24 (17.44)	88.11 (17.80)
Pain rating	Mean (SD)	2.46 (1.43)	2.55 (1.18)
Compulsive Behavior Checklist total score	Mean (SD)	4.12 (3.99)	2.67 (3.16)
Total sleep problem score	Mean (SD)	12.03 (9.15)	11.67 (8.54)

Table 1. Participant characteristics for the Cornelia de Lange syndrome and Comparison groups

Table 2. Operational definitions of individual topographies of self-injurious behaviours

BEHAVIOUR	OPERATIONAL DEFINITIONS
Body to object banging	Movement of the hand or body part down onto and making contact with an object (excluding body throwing and slapping surface).
Body-hitting	Movement of the hand or object down onto and making contact with the trunk of the body.
Body-picking	Sweeping motion of the finger nail(s) to scratch or digging motion to pick at the body.
Body-poking	Pressing the tip of a single finger or thumb into the body.
Body-throwing	Movement of the body down into a sitting position so that the back and/or bottom make contact with a surface.
Ear-poke	Any finger or thumb inserted into ear canal.
Elbow-flicking	Rapid sweeping movement in which the elbow sweeps and makes contact with the edge of a surface.
Eye-poking.	Pressing the tip of a single finger or thumb into the eye socket.
Face poking	Pressing the tip of a single finger or thumb into the face or jaw-line (including dressing).
Face-hitting.	Movement of the hand or object down onto and making contact face.
Face-picking	Sweeping motion of the finger nail(s) to scratch or digging motion to pick at face including cheek and jaw line.
Finger insertion	Finger(s) inserted into small non-bodily orifices.
Hair-manipulation	Actively manipulating hair or scalp with fingers e.g. pulling and twisting and scratching scalp.
Hand-biting	Enclosing and clamping teeth down onto fingers, hand or arm.
Head-bang	Movement of head towards and making contact with a surface (e.g. tables, walls, floor).
Head-hitting	Movement of the hand or object down onto and making contact with the head.
Lip-biting	Teeth clamped down over lip.
Mouth-flicking	Pushing finger(s) so that they move from between the teeth rapidly out of mouth.
Neck-picking	Sweeping motion of the finger nail(s) to scratch or digging motion to pick at the neck.
Picking-hands/arms	Sweeping motion of the finger nail(s) to scratch or digging motion to pick at hands, fingers or arms.

	Number of individuals showing behaviour (Percentage)		Odds Ratio	95% Confidence Interval	
	CdLS Group	Comparison Group		Lower	Upper
Self-injury	30 (55.6)	19 (41.3)	1.78	0.80	3.94
Physical Aggression	17 (31.5)	22 (47.8)	0.50	0.22	1.13
Verbal Aggression	0 (0.0)	7 (15.2)	0.05	0.00	0.87
Destruction of Property	22 (40.7)	15 (32.6)	1.42	0.63	3.23
Inappropriate Vocalisations	19 (35.2)	19 (41.3)	0.77	0.34	1.73

Table 3. Prevalence of clinically significant self-injury and other behaviour disorders in the Cornelia de Lange and Comparison groups with odds ratios and 95% confidence intervals.

	Percentage of individuals showing behaviour		Chi-Square	p
	CdLS (N=53)	Comparison (N=42)		
Topographies of SIB				
Biting	56.6	33.3	5.10	.02
Body to object	28.3	21.4	.58	.44
Skin picking	75.5	61.9	2.03	.15
Body poking	20.8	28.6	.78	.38
Striking	28.3	28.6	.01	1.00
Target of SIB				
Body	64.2	50.0	1.93	.16
Face	67.9	59.5	.72	.40
Head	30.8	23.8	.56	.45
Hand	75.5	40.5	11.96	.001
Mouth	11.3	2.4	2.74	.10
Target of body contact stereotyped behaviour				
Body	62.3	28.6	10.67	.001
Face	98.1	95.2	.63	.43
Head	86.8	40.5	22.5	<.001
Hand	96.2	97.6	.15	.70
Mouth	42.1	52.0	.42	.51
Topographies of noncontact stereotyped behaviour				
Body rocking	22.6	41.5	3.84	.05
Body spinning	17.0	14.6	3.84	.76
Hand flapping	50.9	42.9	1.73	.42
Hand posturing	45.3	11.9	12.31	<.001
Other behaviour disorder				
Physical aggression	17.0	31.0	2.57	.11
Verbal aggression	0.0	2.4	1.28	.26
Destruction of property	45.3	50.0	0.21	.65
Any behaviour disorder	35.8	64.3	7.59	.006

Table 4. Prevalence of operationally defined behaviours seen at observation occurring more than once for the Cornelia de Lange and Comparison groups.

	CdLS		Comparison		Mann-Whitney U	P
	N	Median	N	Median		
All SIB	29	2.36	17	3.66	242.50	.93
Topographies						
Picking	24	1.03	17	.39	169.50	.36
Poking	8	.45	9	.10	26.00	.37
Striking	13	.10	7	.23	37.50	.54
Biting	19	.58	11	.98	102.00	.93
Body to object	11	.06	7	.03	35.00	.79
Target						
Body SIB	22	.10	13	.14	120.00	.45
Face SIB	22	.18	17	.15	179.00	.83
Head SIB	14	.10	8	.11	53.50	.87
Hand SIB	25	1.77	15	.80	182.00	.89
Mouth SIB	2	.24	0	0	-	-

Table 5. Median percentage of time operationally defined behaviours seen at observation in participants from the Cornelia de Lange and Comparison groups who showed self-injurious behaviour.

Study	N	Reported prevalence rates of		
		Self-injury	Physical aggression	Destruction of property
Present study – questionnaire	54	56%	32%	41%
Present study - observations	54	93%	17%	45%
Beck (1987)	36	17%	not measured	not measured
Gualtieri (1990)	13	64%	41%	10%
Berney <i>et al.</i> (1999)	49	55%	10%	33%
Sarimski (1997)	27	40%	not measured	7%
Hyman <i>et al.</i> (2002)	88	64%	43%	53%

Table 6: A comparison of previous findings of prevalence rates for behaviour disorder in Cornelia de Lange Syndrome with results from this study.