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Sleep disorders in children with Angelman and Smith-Magenis syndromes: The assessment of potential causes of disrupted settling and night time waking

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Abstract

Background: Sleep problems are common in Smith-Magenis (SMS) and Angelman syndromes (AS). Effectiveness of interventions depends on appropriate assessment, complicated by compromised self-report and health and behaviour difficulties. Studying settling and waking in these syndromes could inform assessment.

Aims: To describe settling and waking behaviours in children at high-risk of sleep and health problems, using direct observation.

Methods and Procedures: Video and actigraphy data were collected for 12 participants with AS (*Mean* age = 8.02, SD = 2.81) and 11 with SMS (*Mean* age = 8.80, SD = 2.18). Settling (30 minutes prior to sleep onset) and night waking were coded for nineteen behaviours relating to pain, challenging behaviour and caregiver interaction. Lag sequential analyses were conducted for pain-related behaviours.

Outcomes and Results: Percentage of time spent in behaviours was calculated. Parent-child interactions (0.00-9.93%) and challenging behaviours (0%) were rare at settling and waking in both groups. In the AS group, pain-related behaviours were more likely to occur before waking than by chance ($p < 0.001$).

Conclusions and Implications: Findings highlight the importance of considering pain as a cause of sleep problems in Angelman syndrome. The principle and methodology could be extended to people with ID experiencing sleep problems.

Keywords: Sleep, Smith-Magenis syndrome, Angelman syndrome, actigraphy, video coding, pain

What this paper adds?

This is the first description of behaviours shown by children with Smith-Magenis and Angelman syndromes when settling to sleep and when waking at night. It demonstrates the plausibility and utility of videosomnography as a novel assessment approach in these groups, pairing objectively defined settling and waking periods with night-vision footage.

By identifying the temporal association of pain-related behaviours with settling and waking periods, the findings highlight the need for pain and discomfort to be considered in the assessment of sleep problems in individuals with intellectual disability. Critically, this consideration of internal factors should occur before trialling interventions based on extinction or sleep hygiene procedures.

Settling and waking behaviours in children with Angelman and Smith-Magenis syndromes

1. Introduction

Specific sleep disorders and impaired quality, timing and duration of sleep are more common in individuals with intellectual disability (ID) than those of typical development (TD) (Surtees, Oliver, Jones, Evans & Richards, 2017; Tietze et al., 2012). In ID a higher prevalence of sleep disorders is associated with cause of intellectual disability, such as the presence of a specific genetic syndrome (Surtees et al., 2018). In addition to elevated risk of sleep disorders across rare syndromes, a recent meta-analysis Agar, Brown, Coulborn, Oliver, & Richards (2019) reveals contrasting prevalence rates of specific sleep disorders *between* rare genetic syndromes, conferring evidence of syndrome-related risk for particular sleep disorders.

Poor sleep has diverse detrimental effects on TD individuals, including impaired concentration and memory consolidation (Fallone, Acebo, Seifer, & Carskadon, 2005; Stickgold, 2005). In those with Down syndrome (DS), poor sleep is associated with compromised learning and executive functioning (Ashworth, Hill, Karmiloff-Smith & Dimitriou, 2015; Chen, Spano & Edgin, 2013). Additionally, in people with ID and autism poor sleep is associated with daytime challenging behaviour (Cohen et al., 2017). Finally, poor sleep in children with ID is associated with poorer parent sleep quality, greater parent stress and lower mood in caregivers (Richdale, Francis, Gavidia-Payne, & Cotton, 2000; Chu & Richdale, 2009). Thus, intervention for poor sleep is essential for those with ID and their caregivers.

As in TD groups, effective sleep intervention in ID is predicated on robust identification of the cause of sleep disorder. Once aetiology is identified, appropriate interventions are available for specific sleep disorders in people with ID, for example recommendations for

proactive screening and treatment for obstructive sleep apnea (OSA) in individuals with DS (Bull & the Committee on Genetics, 2001; Nation & Brigger, 2017) and calls to implement behavioural treatments for behaviours associated with operantly maintained insomnia in individuals with ID (Wiggs & France, 2000). However, the implementation of these interventions in the high-risk population of people with ID is reliant on careful clinical description of the nature and putative cause of the sleep problem.

The differing prevalence rates of sleep disorders between rare genetic syndromes (Agar et al., 2019) allude to divergent phenotypic drivers for some sleep disorders. For example, the frequently reported high prevalence of OSA in individuals with DS has been linked to the cranio-facial characteristics of the syndrome (for an overview, see Churchill, Kieckhefer, Landis, & Ward, 2011). Agar et al. (2019)also demonstrated that other syndromes with similar facial characteristics have an elevated rate of sleep-related breathing difficulties, including Prader-Willi and mucopolysaccharide disorder syndromes. These associations highlight how understanding the mechanism/aetiology of sleep disorder in one syndrome group can inform understanding of mechanism/aetiology in other syndrome groups.

Alongside physical phenotypic characteristics that underpin poor sleep in people with rare syndromes, other potential causes include the individual's sleeping environment (Jan et al., 2008), caregiver-child interactions and child health problems which may all also be influenced by the behavioural phenotype associated with the syndrome. Additionally, anxiety or pain may contribute to sleep difficulty (Rzepecka, McKenzie, McClure & Murphy, 2011; Breau & Camfield, 2011). Chronic pain in particular is a known correlate of poor sleep in TD individuals (Long, Krishnamurthy, & Palermo, 2008) and is common in people with rare syndromes due to elevated rates of health problems (Waite et al., 2014; Berg et al., 2007). Identification of painful health conditions as a cause of sleep problems is a prerequisite of effective and ethical sleep interventions for people with rare syndromes associated with ID.

However, pain is very difficult to assess directly in those who cannot accurately self-report (McGuire, Daly, & Smyth, 2010; Foley & McCutcheon, 2004). Thus, current approaches to assessment of cause for specific sleep problems in those with rare syndromes associated with ID is limited by the validity and relaibility of the measurement of potential causes such as pain.

More generally, appropriate assessment of the poor sleep is challenging for people with ID. For example, typical methods of assessing insomnia include self-report about sleep or keeping a sleep diary (Buysse, Ancoli-Israel, Edinger, Lichstein, & Morin, 2006). These methods may not be appropriate for individuals who are non-verbal or unable to accurately describe their internal state (Emerson, Felce & Stancliffe, 2013). Where carers are asked to keep a sleep diary on behalf of individuals with ID, recall may be limited due to sleep deprivation, or reduced proximity to the person (Short, Gradisar, Lack, Wright, & Chatburn, 2013). Thus parent-report may be an unreliable method of measuring sleep in individuals with ID. The gold standard of sleep assessment is polysomnography (PSG), but this is usually conducted in a sleep laboratory and may not be tolerated by people with ID (Ashworth, Hill, Karmiloff-Smith & Dimitriou, 2013). Recent studies have therefore used actigraphy, an objective measure of sleep quality with greater ecological validity than PSG (Van de Water, Homes & Hurley, 2011). However, whilst this provides robust objective description of sleep/wake parameters, recording via actigraphy alone gives limited insight into the potential cause of poor sleep, including pain or discomfort as discussed above. In TD infants, video recordings have been valuable in assessing sleep behaviours, environments and interactions (see Teti, Kim, Mayer & Countermine, 2010; Kim, Stifter, Philbrook & Teti, 2014) but as yet there are no studies using night-time video recordings in individuals with ID.

Therefore one approach to progress accurate sleep assessment and description of possible cause, is to combine objective sleep assessment via actigraphy with fine-grained behavioural

observation. A novel approach would be to describe child and parent settling and waking behaviours via recordings on night-vision cameras in children with ID who have a sleep problem, using identification of sleep/wake parameters as defined by actigraphy. Settling and waking are crucial to our understanding of behavioural insomnia (International Classification of Sleep Disorders 3, American Academy of Sleep Medicine, 2014) and yet there are no current studies which describe settling and waking in individuals with rare genetic syndromes associated with ID despite the heightened risk. By studying behaviours during the settling period, it will be possible to identify potential for improved sleep hygiene, operantly maintained signalling behaviours (such as crying), and existing self-settling behaviours which may form part of a behavioural intervention. Careful delineation of behaviours during night waking confers an opportunity to identify possible causes of waking (e.g. behaviours indicative of pain due to health conditions) and assess the extent to which carers are involved in re-settling to sleep after waking. This is important for carer wellbeing and also for understanding the maintenance of behavioural insomnia.

To provide a comprehensive description of potentially problematic settling and waking behaviours, the current study recruited children with AS and SMS, whose parents reported that they had a 'sleep problem'. Both syndromes are associated with a high prevalence of sleep difficulties (Pelc, Cheron, Boyd & Dan, 2008; Edelman et al., 2007), over and above that of estimates for individuals with heterogeneous ID (Tietze et al.,2012; Agar et al., 2019). Both have unique but well-described phenotypes (for an overview see: Horsler & Oliver, 2006; Smith, Dykens & Greenberg, 1998) with characteristics which likely contribute to sleep difficulties. In SMS, the predominant explanation for individuals' poor sleep, particularly early morning waking and excessive daytime sleepiness, is a biological difference in the release pattern of the hormone melatonin (Potocki et al., 2000; DeLeersnyder et al., 2001) In comparison to TD individuals, individuals with SMS are

reported to have an 'inverted' melatonin release pattern, which peaks during the day and falls during the night, thought to be a by-product of dysregulation of the retinoic acid-induced 1 gene, which is either deleted or mutated in SMS (Falco, Amabile & Acquaviva, 2017). In individuals with AS, biological explanations of poor sleep are less developed, but associations have been made with the elevated prevalence of epilepsy in this group (Conant, Thibert & Thiele, 2009) and some evidence of differences in melatonin serum levels and secretion patterns (Takaesu, Komada & Inoue, 2012; Paprocka et al., 2017).

In addition, both groups have a high prevalence of painful health conditions including constipation, otitis media, gastrointestinal reflux and scoliosis (Gropman, Duncan & Smith, 2006; Dagli, Mueller, & Williams, 2015, Glassman et al., 2017) which have been linked to poor sleep in TD individuals and individuals with autism (Krakowiak, Goodlin-Jones, Hertz-Picciotto, Croen & Hansen, 2008; Horvath & Perman, 2002; Buie et al., 2010, Mannion, Leader & Healy, 2013, Trickett, Heald, Oliver & Richards, 2018). Individuals with both syndromes also show strong preference for caregiver attention (Oliver et al., 2007; Wilde, Sliva & Oliver, 2013) which may lead to multiple interactions with caregivers at night. As such, they provide credible exemplars in which to examine the contribution of child, and parent-child behaviours to sleep parameters.

The primary aim of the current study is to describe behaviours, including those linked to pain, observed during periods of settling to sleep and night waking identified via actigraphy, for children at high-risk of sleep problems. A secondary aim is to examine the utility of these behavioural data to contribute to the identification of the cause of poor sleep in these groups.

2. Methods

2.1. Participants

Paired video and actigraphy data ('videosomnography') collected for 23 participants (see Table 1) as part of a wider study conducted by Trickett and colleagues in 2015-2016 were analysed. In the wider study, 20 children with AS and 20 with SMS who had a parent-reported sleep problem were recruited through an existing database of families who had provided consent to be contacted about research studies, or through the relevant family support groups. All children wore an actiwatch for a week long at-home sleep assessment, with cameras placed in their bedrooms. During the study week parents also completed a battery of questionnaires and the Vineland Adaptive Behavior-2 Interview schedule over the phone or in person with a trained researcher. The 23 children reported here are those where at least one night of actigraphy data could be paired with the corresponding night's video footage.

Twelve participants with AS (*M* chronological age = 8.02, 6 males) and 11 with SMS (*M* chronological age = 8.80, 7 females) were included. In the AS group, parents reported a mode household income of £65,001 or more per year (range: less than 15,000 - £65,001 or more per year). In the SMS group, mode household income was between £45,001 and £65,000 per year (range: £25,001 - £65,001 or more per year). As expected, children with SMS showed higher levels of adaptive functioning measured by the Vineland Adaptive Behavior-2 Interview (*M*=65.90, *SD*=11.44) than children with AS (*M*=47.16, *SD*=7.94). Sleep was objectively poor in both groups with increased wake after sleep onset and reduced total sleep time in the SMS group compared to chronologically age-matched TD peers and decreased sleep efficiency (time spent in bed actually sleeping) in the AS group compared to chronologically age-matched TD peers reported in the wider cohort (Trickett et al., 2019a; 2019b).

All but two participants in the study had experienced a health problem in the past month prior to the recordings being taken (one participant with SMS reported no recent

health problems and the other, also with SMS, did not complete this questionnaire). The most common problems were skin problems (n=13) such as eczema and psoriasis, ear infections/glue ear (n=9) and bowel problems such as constipation (n=9).

Table 1. *Participant Characteristics*

Participant	Gender	Chronological Age	Vineland Adaptive Behavior Score	Nights of footage	Nights of Actigraphy	*M* Total Sleep Time (hh:mm:ss)	*M* Wake After Sleep Onset (minutes)	*M* Sleep Efficiency (%)	Use of Melatonin
AS1003	Male	5.52	47	6	7	08:31	18.07	93.37	N
AS1006	Male	7.54	55	6	6	07:47	164.58	71.33	N
AS1008	Male	7.54	53	6	6	07:40	117.71	74.37	Y
AS1009	Female	13.21	34	4	9	07:34	105.00	77.43	N
AS1010	Male	12.72	32	5	5	07:54	58.60	69.61	Y
AS1012	Female	4.01	50	6	8	10:16	56.81	85.07	N
AS1014	Female	9.64	43	7	8	07:39	64.13	82.28	Y
AS1019	Male	5.83	44	7	7	10:14	77.86	86.71	N
AS1022	Male	4.65	51	7	8	07:20	126.81	73.79	Y
AS1023	Female	10.07	46	6	7	08:11	189.36	68.86	Y
AS1025	Female	7.65	57	7	7	07:54	140.07	70.07	Y
AS1026	Female	7.8	54	6	7	09:08	124.29	78.80	N
Mean (SD)	6:6	8.02 (2.81)	47 (7.60)	6 (0.86)	7 (1.04)	08:20	103.60	77.64	6:6
SMS1003	Male	7.66	69	6	6	08:21	74.31	85.99	N
SMS1005	Female	10.15	63	7	9	08:34	98.75	79.09	M
SMS1011	Female	7.82	71	6	7	06:50	38.57	87.90	Y
SMS1012	Female	5.97	64	6	7	08:41	137.58	78.30	N
SMS1014	Female	9.14	69	6	7	05:03	108.64	71.39	~
SMS1021	Male	7.85	81	6	9	07:49	196.81	69.10	Y
SMS1022	Female	8.26	71	4	8	08:59	30.81	90.25	Y
SMS1024	Female	9.06	43	7	9	06:49	60.44	76.84	Y
SMS1025	Male	14.84	47	5	5	05:48	79.80	81.02	Y
SMS1027	Female	7.31	73	1	7	07:03	39.90	87.67	Y
SMS1037	Male	8.74	74	2	7	06:54	48.31	84.92	Y
Mean (SD)	4:7	8.8 (2.18)	66 (10.91)	5 (1.89)	7 (1.23)	07:21	83.08	81.13	6:2:1

Vineland Adaptive Behavior Score calculated as a composite of subdomain scores on the Vineland Adaptive Behavior-2 Interview schedule relating to receptive, expressive and written communication, daily living skills, interpersonal relationships, play and leisure skills, coping skills and gross and fine motor skills. AS refers to a participant with Angelman syndrome, SMS refers to a participant with Smith-Magenis syndrome. Y = Yes, N = No, ~ = Occasional use of Melatonin, M = Missing data.

2.2. Videosomnography

Children were recorded overnight in their own homes using night-vision cameras, while wearing the Actiwatch 2 (Philips Respironics) on their non-dominant wrist or ankle. The Actiwatch 2 is an accelerometer which defines sleep and wake based on movement in 30

second epochs. Data were downloaded to Philips Actiware software and analysed using the protocol developed by Trickett et al (2017). This is a standardised protocol designed to remove artefact from the data which can make actigraphy less reliable (Acebo et al., 1999), for example by excluding periods where the actiwatch was removed.

One static infra-red camera was installed in each child's bedroom for the duration of the study week. Cameras were positioned to optimise capture of footage of the child whilst in the bedroom, including the bed and as much of the bedroom as possible. Cameras were placed in the ceiling corner where possible, dependent on the set-up of child's bedroom. Parents were instructed only to record children at night and turn the camera off in the morning. Prior to clipping, night-vision footage was checked for quality. Footage which was very unclear or pixelated, footage which could not be opened, and footage where the child could not be seen (e.g. camera pointed in the wrong direction) was excluded at this stage.

For each child, the settling period for each night of the study was clipped from the usable camera recording of each night. This period was defined as the final 30 minutes before the child fell asleep according to actigraphy. Up to five wakings per child per night were also clipped. A waking was defined as a period of movement identified by actigraphy after the onset of sleep. Each waking was distinct in that the actigraphy indicated that the child had fallen asleep and then had subsequently woken. The 10 minutes prior to and 20 minutes following this waking time was clipped from the usable night-vision camera recording. The child may or may not have resumed sleep during the following 20 minute period (see Figure 1 for an outline of this procedure). The final waking of each night (i.e. the time the child awoke for the day) was not clipped. The total number of clips was 171 (5,130 minutes).

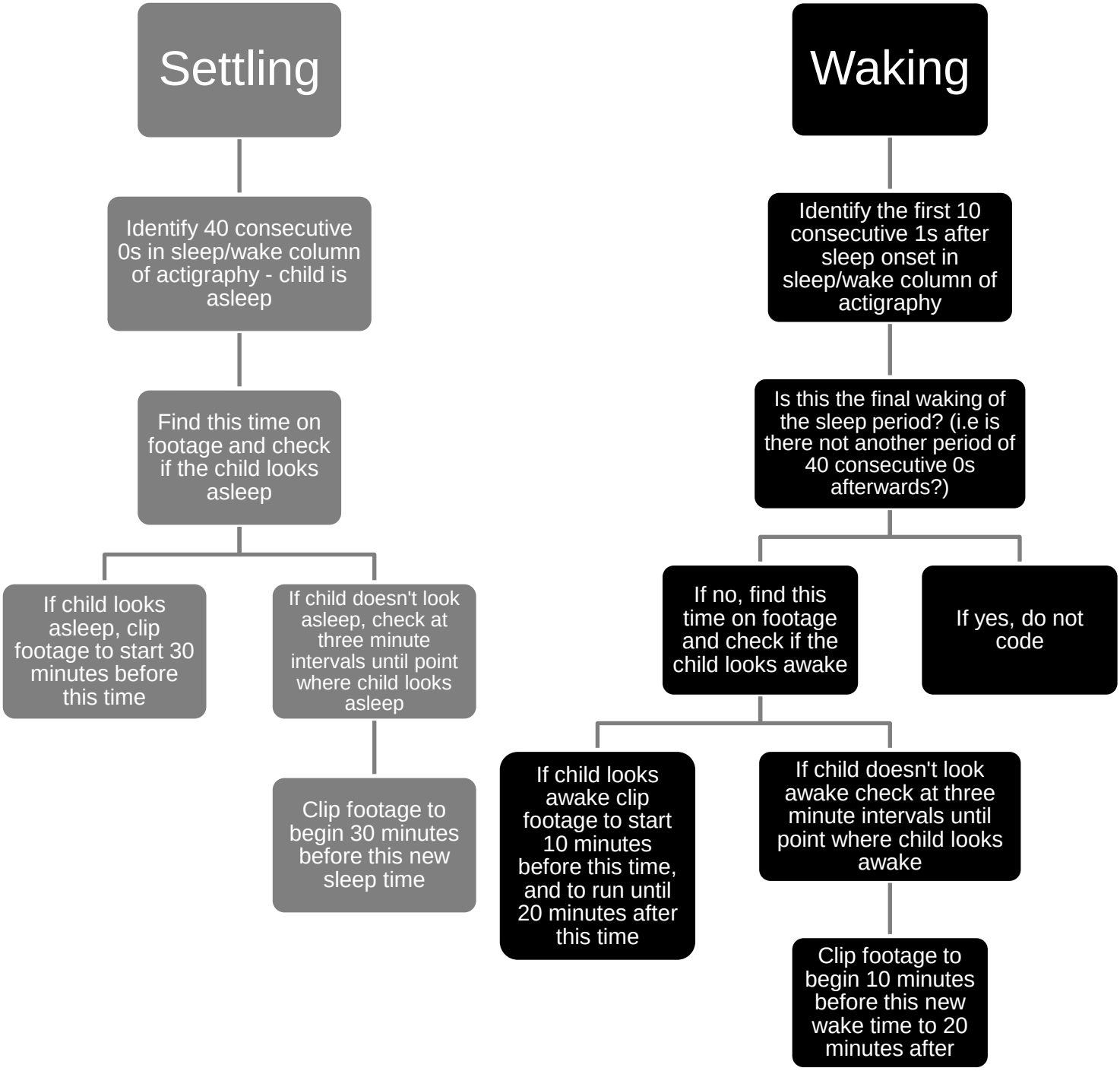

Figure 1. The sampling process of clips for videosomnography.

2.3. Coding

Nineteen behaviours relating to child pain, activity, challenging behaviour and interactions with caregivers were coded for all participants by the first author. Codes were

derived initially through identification of informant-report tools that measured the relevant constructs with high reliability and validity. For example, the Face, Legs, Activity, Crying and Consolability (FLACC: Merkel, Voepel-Lewis, Shayevitz & Malviya, 1997) and The Non-Communicating Child Pain Checklist-Revised (NCCPC-R: Breau, McGrath, Camfield, & Finley 2002), which measure pain, and the Challenging Behaviour Questionnaire (CBQ; Hyman, Oliver & Hall, 2002). Operationalised behavioural codes were then developed from items on these informant-report measures (see Table 2), for example the 'Self-Injurious Behaviour', 'Aggression' and 'Destructive Behaviour' codes were derived from items on the CBQ. Codes were derived from the Face, Legs, and Crying subscales of the FLACC and the Vocal and Facial subscales of the NCCPC-R to observe possible indicators of pain – coded as 'Jerking/Restless Legs' and 'Negative Vocalisations and Affect'.

Behaviours were coded using ObsWin, a real-time coding programme developed by Martin, Oliver and Hall (2000). ObsWin allows the observer to code operationally defined behaviours as distinct occurrences ('event behaviours' – for example coughing), or episodes of continuous behaviour ('duration behaviours' – for example lying down) by coding the onset and offset of these behaviours. The full coding scheme is outlined in Table 2.

To assess inter-rater reliability, 37 clips of the 171 (22%) were coded by an independent second observer. These clips included a proportional number of settling and waking periods for each syndrome, so that as there were more clips of individuals with Angelman syndrome, and more clips of individuals at waking in both groups, a greater number of these were included in the reliability set. Kappa coefficients were calculated for all coded behaviours at three second intervals. Reliability was good (mean $\varkappa = 0.72$; range 0.52-0.95).

Table 2. *Operational definitions of coded behaviours.*

Behaviour	Kappa coefficient	Variable	Definition
Self-Injurious Behaviour	Not seen	Duration	Any non-accidental behaviour initiated by an individual towards themselves which causes undesirable physical change or damage (e.g. hitting, biting, poking, scratching, pulling self).
Aggression	Not seen	Duration	Any non-accidental behaviour initiated by an individual towards others which causes undesirable physical change or damage (e.g. hitting, biting, poking, scratching, pulling self). Also include verbal aggression.
Destructive Behaviours	Not seen	Duration	Any non-accidental behaviour initiated by an individual which causes undesirable physical change or damage to the environment (e.g. breaking windows, tearing clothing, throwing toys etc).
Non-Verbal Communication	0.71	Duration	The individual signs/gestures/points or leads another individual towards something, in order to communicate something to them. This may involve hugging or guiding the other individual's body physically.
Verbal Communication	0.80	Duration	The individual speaks to or calls another individual. The verbal communication may be intelligible or unintelligible.
Rocking	0.71	Duration	Instances where the individual moves their head, upper body, or entire body from left to right or forwards and backwards in a rhythmical manner.
Repetitive Hand Movements (RepHand)	0.67	Duration	Repeated manipulation of the hands (e.g. tapping fingers) or items in the hand (e.g. twiddling or tapping objects).
Interaction with Toys (InteractToys)	0.63	Duration	Instances where the individual engages with a toy, activity or play object. This may include talking to the toy (this communication may be intelligible or non-intelligible), picking it up, playing with it etc.
Interaction with iPad/other device (InteractDevice)	0.95	Duration	Instances where the individual engages with an electronic device, by picking it up or touching the screen etc. This also includes instances where the child is looking at a device (e.g. watching a film or TV).
Jerking/Restless Legs (Legs)	0.52	Event	Prolonged and significant movement of the legs, such as a sharp kicking movement or consistent fidgeting. NB: This does not include kicking which is intentionally directed at an object or individual (code as destruction/aggression). If the behaviour stops for 5 seconds, the next bout should be coded as a new event. If the behaviour stops for less than 5 seconds, this would be included in the original event.

Coughing	0.83	Event	Instances where the participant expels air suddenly, with a harsh noise. If the behaviour stops for 5 seconds, the next bout should be coded as a new event. If the behaviour stops for less than 5 seconds, this would be included in the original event.
Drinking	0.73	Event	The individual sips liquid from a cup or bottle. If the behaviour stops for 5 seconds, the next bout should be coded as a new event. If the behaviour stops for less than 5 seconds, this would be included in the original event.
MouthSuck	0.58	Duration	Instances where the individual chews objects/clothing/hand, or places them in their mouth. Include instances where the individual repeatedly places their mouth and lips around their own thumb, hand or fingers, or a dummy.
Bruxism	Not seen	Duration	Instances where the individual is seen to be grinding their teeth and clenching their jaw. This may include instances where the individual's chin quivers.
Negative Vocalisations and Affect (NegVocAffect)	0.60	Duration	Facial expressions and vocalisations that look/sound distressed or negative in their intonation. This can include groaning, crying, gasping, grunting, loud sharp cries, furrowing brow, pursing lips. NB: This does not include verbal communication (intelligible/non-intelligible).
Positive Vocalisations and Affect (PosVocAffect)	0.64	Duration	Facial expressions and vocalisations that look/sound happy or positive in their intonation, such as laughing, giggling etc. NB: This does not include verbal communication (intelligible/non-intelligible).
Rise Up	0.74	Event	Instances where the individual moves from a lying down position to sitting upright in bed/standing/kneeling.
Lying Down	0.84	Duration	Instances where the individual is clearly awake (i.e. eyes open, or making some noise) but is lying down in a sleeping position in their bed.
Presume Sleep	0.85	Duration	Instances where the individual is quietly lying down in a sleeping position in their bed for at least a minute, with their eyes closed if the face is visible.

2.4. Data Analysis

To describe the settling and waking behaviours of children with SMS and AS, percentage intervals of coded behaviours were calculated, with sections where footage was 'uncodeable' filtered out[2]. For each behaviour, the total number of intervals (seconds) where this occurred in each group was divided by the total number of intervals coded in all settling clips and waking clips for each group, and also the total number of intervals across all types of clip for each group (combined). This approach was taken over calculating frequency of behaviours as it allows researchers to compare both event and duration behaviours in the same analysis.

In order to address the second aim, restricted lag sequential analyses for each group were conducted to further investigate the specific role of pain-related behaviours (a combination of pain-related leg movements, negative vocalisations and negative affect with definitions derived from the FLACC and NCCPC-R) in settling and waking. Lag sequential analyses were used to explore temporal relationships between the coded behaviours and falling asleep or waking up by comparing unconditional probabilities of the target behaviours occurring (e.g. the probability of leg movements occurring in all observation periods) to the conditional probabilities of target behaviours occurring *given* the criterion of falling asleep or waking up (e.g. the probability of leg movements *given* that the children have just woken up). A z score indicates whether the unconditional and conditional probabilities differ significantly, typically evidenced by a z score of 1.96 or above (Moss et al., 2005). However, to avoid type 1 errors this cut-off was increased to 3.10, $p < 0.001$. Lags were examined for 60 second intervals for 20 minutes prior to falling asleep, and for 10 minutes before and 10 minutes after waking. Lag zero indicates occurrence of the criterion behaviour.

3. Results

[2] Uncodeable footage refers to instances where the individual was no longer visible to be coded, e.g. because they had left the room or the range of the camera. These proportions of clips were filtered out for analysis.

3.1. Describing settling and waking

To address the first aim of the study, the percentage of intervals where each behaviour occurred was calculated for settling and waking clips, pooled across all participants in each syndrome group. The results in Table 3 demonstrate that several behaviours (including all three forms of challenging behaviour) were not observed in any clips. Others, such as coughing and drinking, occurred in very few percentage intervals.

Table 3. *Percentage of intervals where behaviours occurred across settling and waking*

Clip (Number of intervals)	Angelman Syndrome (n=12)			Smith-Magenis Syndrome (n=11)		
	Settle (39362)	Wake (121265)	Combined (160627)	Settle (34623)	Wake (71043)	Combined (105666)
Coughing	0.01	0.01	0.01	0.01	0.01	0.01
Drinking	0.13	<0.01	0.00	0.00	0.00	0.00
Interact with Device	9.23	0.00	2.26	26.38	0.57	9.02
Interact with Toys	10.75	0.26	2.83	11.35	1.98	5.05
Jerking/Restless Legs	0.43	0.54	0.51	0.33	0.22	0.25
LyingDown	69.09	42.07	48.69	54.46	37.98	43.38
Mouthing/Sucking	9.76	4.26	5.60	0.57	1.46	3.00
Negative Vocalisations and Affect	1.96	2.31	2.22	0.57	0.03	0.21
Non-verbal Communication	1.00	0.11	0.33	1.04	0.01	0.34
Positive Vocalisations and Affect	0.46	<0.01	0.12	0.17	<0.01	0.06
PresumeSleep	19.04	52.39	44.21	28.61	54.88	46.27
Repetitive Hand Movements	0.12	0.43	0.35	0.79	0.18	0.38
RiseUp	0.24	0.06	0.10	0.18	0.09	0.12
Rocking	1.36	1.11	1.17	0.22	7.41	5.05
Verbal Communication	0.05	0.00	0.01	9.93	3.68	5.73

Table 3 indicates that at settling, participants with AS and SMS spent the majority of the time lying down (69.09% and 54.46% of intervals respectively). Both groups spent time interacting with toys (10.75% and 11.35%) and devices, particularly the SMS group (26.38%). Children with AS spent 9.76% of the settling period mouthing and 1.36% rocking. Children with SMS spent less time showing these behaviours, but a greater percentage of time was spent in verbal communication with a carer (9.93%).

At waking, children with AS continued to show some evidence of mouthing and rocking behaviours and children with SMS engaged in these behaviours more than at settling (1.46% mouthing and 7.41% rocking). Notably, both groups spent little time in non-verbal or verbal communication once they had woken, and few interactions with toys (0.26% and 1.98%) or devices (0% and 0.57%) were observed.

Some evidence of potentially pain-related behaviours were seen in both groups at settling and waking, in particular the AS group who spent 1.96% and 2.31% of the time crying or showing negative affect at settling and waking respectively.

3.2. Lag analyses

To address the second aim of the study, group lag analyses were conducted to further investigate the specific role of pain-related behaviours (a combination of pain-related leg movements, negative vocalisations and negative affect with definitions derived from the FLACC and NCCPC-R) in settling and waking.

Figure 2 displays the unconditional probability of each group engaging in leg movements and negative vocalisations and affect at settling, and the conditional probability of each group engaging in these behaviours *given* that they fall asleep. The data indicate that children with SMS and AS are more likely to show pain-related behaviours *given* that they fall asleep shortly afterwards, as there were significant differences between the conditional and unconditional probabilities in both groups during settling periods. Most notably, children in the AS group were more likely to show leg movements in the 16-20 minutes before they fell asleep than the unconditional probability of these movements. Additionally, these behaviours became significantly less likely in the minutes prior to sleep onset in both groups, suggesting that their absence is associated with successful sleep onset.

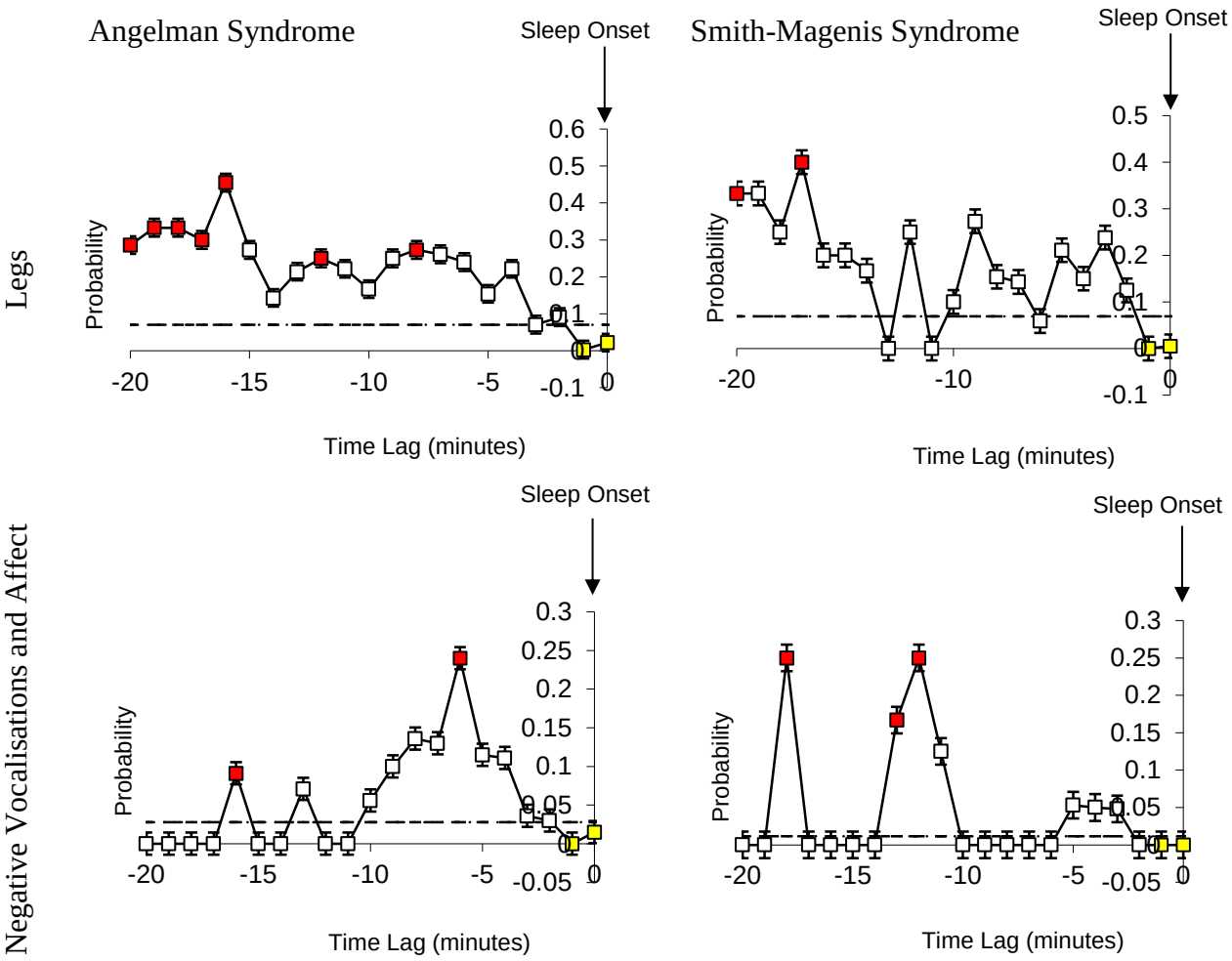

Figure 2. Mean unconditional probability (dashed line) of all children in each group engaging in pain-related behaviours and conditional probability (unfilled squares) of children engaging in these behaviours given that they fall asleep 20 minutes later. Red squares indicate a conditional probability which is significantly higher than the unconditional probability ($z > 3.10$, $p < .001$), yellow squares a conditional probability which is significantly lower than the unconditional probability ($z > -3.10$, $p < .001$).

Figure 3 displays the unconditional probability of each group engaging in leg movements and negative vocalisations and affect at waking, and the conditional probability of each group engaging in these behaviours *given* that they wake at time zero. The figure demonstrates differences between the unconditional and conditional probabilities of these behaviours in both groups at waking. Overall this suggests that the conditional probability of leg movements, negative vocalisations and affect are greater given children have woken at time

zero. For the AS group in particular, the elevated probability of leg movements before waking suggests that children may be waking due to pain evidenced through pain-related leg-movements.

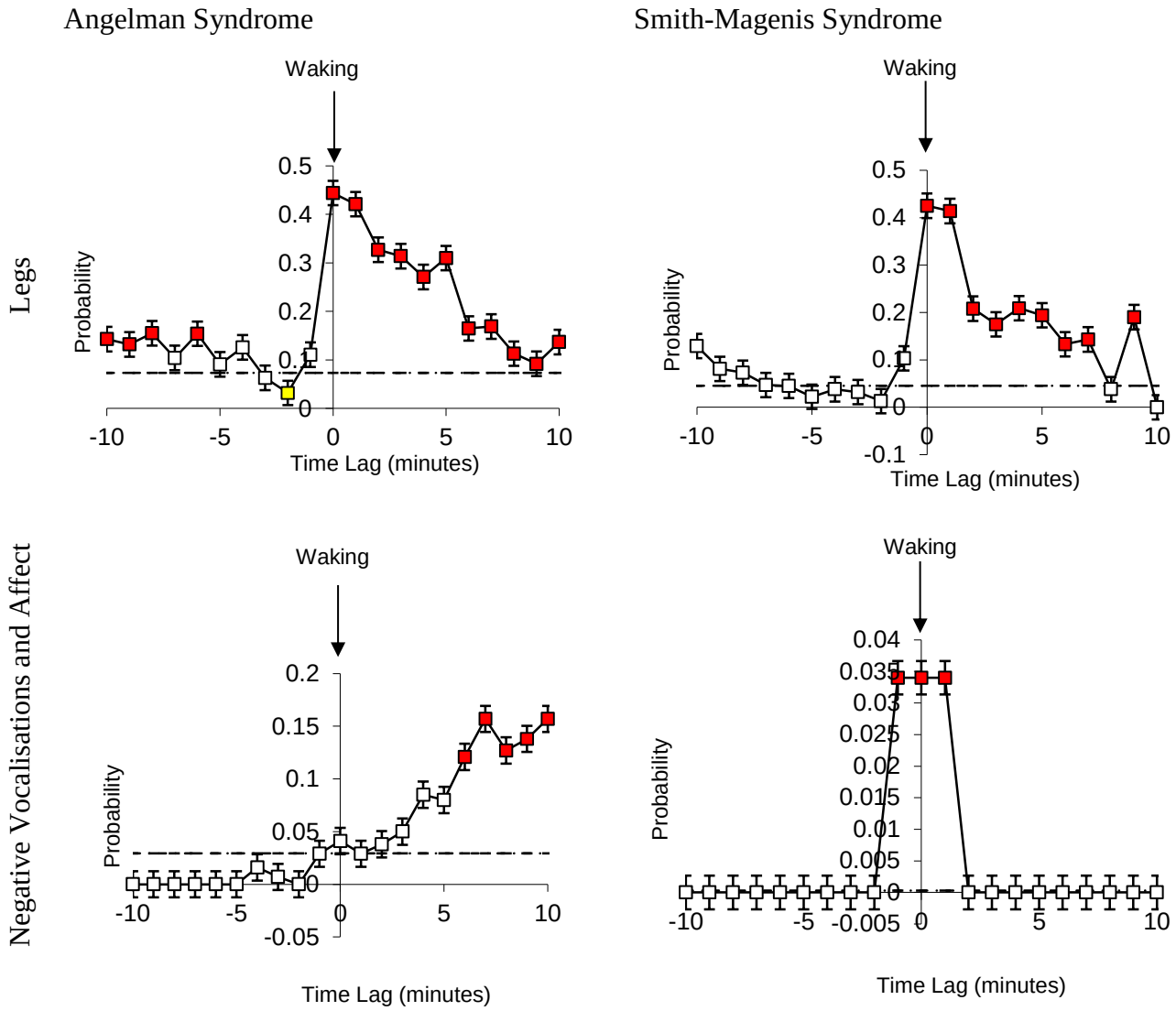

Figure 3. Mean unconditional probability (dashed line) of all children in each group engaging in pain-related behaviours and conditional probability (unfilled squares) of children engaging in these behaviours given that they wake up at time zero. Red squares indicate a conditional probability which is significantly higher than the unconditional probability ($z > 3.10$, $p < .001$), yellow squares a conditional probability which is significantly lower than the unconditional probability ($z > -3.10$, $p < .001$).

In summary, lag analyses at settling indicate that both groups are showing a greater likelihood of pain-related behaviours before they fall asleep than by chance. In the AS group, these pain-related leg movements are also more likely to occur before waking than by chance.

4. Discussion

This study provides the first description of behaviours shown by children with SMS and AS when settling to sleep and waking at night. Crucially, these settling and waking periods were identified via objective sleep assessment, significantly strengthening the validity of the study. An important finding is that these waking and settling periods contain limited evidence of severe behaviour difficulties or potentially associative learning interactions with carers that may contribute to the maintenance of behavioural insomnia. For example, despite the high prevalence of self-injurious behaviour in SMS (92.9%) and elevated rates of physical aggression reported in both groups (Arron, Oliver, Moss, Berg & Burbidge 2011), no challenging behaviour was seen at night time in either group. Furthermore, despite a known preference for social attention in both groups (Oliver et al., 2007; Wilde et al., 2013) children spent relatively little time communicating with others (either verbally or non-verbally) after being put to bed. This suggests that parents are not repeatedly attending to their children at settling or when they wake, supporting informant-report data demonstrating good sleep hygiene in both groups (Trickett et al., 2019a; 2019b). As reducing parent involvement in re-settling is often a key component recommended as part of a behavioural intervention (Vriend & Corkum, 2011; Wiggs & France, 2000), this is important for practitioners to note.

Children spent the majority of the settling and waking periods lying down. There was some evidence of repetitive movements that may be self-soothing, including rocking and repetitive hand movements. Children also spent time interacting with toys and devices, particularly in the settling period. These initial descriptions are important to identifying

behaviours for children which may be amenable to shaping as part of a behavioural intervention for insomnia, and open the possibility of shaping existing self-soothing behaviours as strategies to help children return to sleep after night waking.

Several behaviours which may be indicative of pain were seen in both groups, including leg movements, negative vocalisations and affect. At settling, these behaviours became significantly less likely in the two minutes prior to sleep onset. This suggests these behaviours, which are known characteristics of pain in children with ID and key behavioural indicators used in reliable and valid parent report tools (Merkel et al., 1997; Breau et al., 2002), are associated with disruption to sleep in these groups. The identification of pain-related behaviours during settling and waking is perhaps unsurprising given the high prevalence of painful health conditions in both groups, including constipation, reflux, scoliosis and otitis media (Gropman, Duncan & Smith, 2006; Dagli, Mueller, & Williams, 2015; Glassman et al., 2017). Crucially, the probalistic lag analyses revealed that for children with AS, leg movements potentially indicative of pain were more likely to occur both *before* and after waking. This is in contrast to the SMS group, where the difference in probability of leg movements only occurred after waking. This lends credibility to the hypothesis that suggests pain could be a *cause* of waking in children with AS and requires further investigation.

An alternative hypothesis is that the data here support the notion that children with AS are demonstrating symptoms of restless leg syndrome (RLS) or periodic limb movement disorder (Miano et al., 2005), characterised by the movement of specific muscles in the leg during sleep. The relationship between RLS and periodic limb movement disorder is complicated even in TD populations (see Picchietti & Picchietti, 2008, for an overview) and diagnosis of either typically relies on self-report assessment, thus research in rare syndromes is limited. However, researchers agree that sleep disturbance and characteristic leg

movements can be diagnostic of a specific sleep movement disorder that can be successfully treated (Comella, 2013).

Therefore, whether these movements are due to general pain or RLS it is important that they are identified so that they can be treated. The findings highlight the importance of identifying any underlying *internal* cause of sleep problem (i.e. general pain or RLS which may be waking these children) before applying behavioural intervention techniques to manipulate *external* factors such as parent involvement, the sleeping environment etc. Extinction-based interventions should therefore only be utilised when clinicians are confident that the child is not in pain or discomfort.

The method of videosomnography is both a strength and a limitation of the study. Given that behaviours could only be coded if they occurred on camera, there is the possibility that interactions with caregivers and behaviours of interest may have been missed if children left the bedroom, for example to access a caregiver's attention. This may partly explain the low percentage of communicative behaviours shown by children in Table 3, and highlights the need for future studies to use objective measures to examine parent/child interaction further in these groups at night. However, it should be noted that children only left the bedroom in three settling clips and 14 waking clips (in the SMS group), and no settling clips and one waking clip (in the AS group), thus only 10.53% of all the clips were associated with a child leaving the room. Furthermore, in most cases the child left the room and returned within the coding period, so the window for missed behaviours was limited. Overall the videosomnography method does utilise an objective measure of sleep (actigraphy) to identify the settling and waking periods, thereby allowing the researcher to code behaviours at the relevant time rather than coding an entire night (or week) of footage. This focus on settling and waking is crucial to progressing our understanding of insomnia (Fallone, Owens & Deane, 2002). Though time consuming for the current study, it may be possible to automate

the process of identifying periods of interest (see Schwichtenberg, Choe, Kellerman, Abel & Delp, 2018 for discussion of strengths and limitations of this approach) which would allow future research to more easily observe these critical windows for pain and interaction.

A further limitation of the present study is that the children studied here may not be representative of the wider population of children with AS and SMS, because they were recruited due to a parent-reported sleep problem. Though this approach allows us to thoroughly investigate behaviours potentially associated with the parent-reported sleep problem, we cannot draw firm conclusions about their cause, or the cause of elevated rates of sleep difficulties in these groups as a whole. However, the current study demonstrates that some pain-related behaviours occur in these groups which may indicate that underlying painful health difficulties or discomfort could play a role in poor sleep in AS and SMS. Further work is needed to contrast the behaviours of those with and without a sleep problem in these groups to confirm this association.

In conclusion, this study details the first description of the settling period and night wakings of children with ID, pioneering an objective approach to sleep assessment by combining night-vision camera footage with actigraphy. It is also the first to consider the temporal associations of pain-related behaviours and falling asleep/waking up in children with genetic syndromes at high-risk of sleep and painful health difficulties. Overall the findings highlight the need for pain to be considered as an underlying cause of sleep difficulty before applying sleep hygiene or behavioural intervention principles.

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References

Acebo, C., Sadeh, A., Seifer, R., Tzischinsky, O., Wolfson, A. R., Hafer, A., & Carskadon, M. A. (1999). Estimating Sleep Patterns with Activity Monitoring in Children and Adolescents: How Many Nights Are Necessary for Reliable Measures? *Sleep*, 22(1), 95–103. doi: 10.1093/sleep/22.1.95

G. Agar, C. Brown, S. Coulborn, C. Oliver, C. Richards (2019). The Prevalence and Profile of Sleep Difficulties in Rare Genetic Syndromes: A Meta-Analysis. *Journal of Intellectual Disability Research, 63* (7) 835-836, doi: 10.1111/jir.12662

Arron, K., Oliver, C., Moss, J., Berg, K., & Burbidge, C. (2011). The prevalence and phenomenology of self-injurious and aggressive behaviour in genetic syndromes. *Journal of Intellectual Disability Research*, *55*(2), 109-120.

Ashworth, A., Hill, C. M., Karmiloff-Smith, A., & Dimitriou, D. (2013). Cross syndrome comparison of sleep problems in children with Down syndrome and Williams syndrome. *Research in developmental disabilities*, *34*(5), 1572-1580.

Ashworth, A., Hill, C. M., Karmiloff-Smith, A., & Dimitriou, D. (2015). A cross-syndrome study of the differential effects of sleep on declarative memory consolidation in children with neurodevelopmental disorders. *Developmental Science, 20(2), e12383*.doi:10.1111/desc.12383

Berg, K., Arron, K., Burbidge, C., Moss, J., & Oliver, C. (2007). Carer-Reported Contemporary Health Problems in People With Severe and Profound Intellectual Disability and Genetic Syndromes. *Journal of Policy and Practice in Intellectual Disabilities, 4(2), 120–128*.doi:10.1111/j.1741-1130.2007.00109.x

Breau, L. M., & Camfield, C. S. (2011). Pain disrupts sleep in children and youth with intellectual and developmental disabilities. *Research in developmental disabilities*, *32*(6), 2829-2840.

Breau, L. M., McGrath, P. J., Camfield, C. S., & Finley, G. A. (2002). Psychometric properties of the non-communicating children's pain checklist-revised. *PAIN*, *99*(1–2), 349-357. doi:https://doi.org/10.1016/S0304-3959(02)00179-3

Buie, T., Campbell, D. B., Fuchs, G. J., Furuta, G. T., Levy, J., VandeWater, J., ... & Carr, E. G. (2010). Evaluation, diagnosis, and treatment of gastrointestinal disorders in individuals with ASDs: a consensus report. *Pediatrics*, *125*(Supplement 1), S1-S18.

Bull, M. J. and the Committee on Genetics (2011). Clinical report—health supervision for children with Down syndrome. *Pediatrics 128(2*) *393-406.*

Buysse, D. J., Ancoli-Israel, S., Edinger, J. D., Lichstein, K. L., & Morin, C. M. (2006). Recommendations for a standard research assessment of insomnia. *Sleep*, *29*(9), 1155-1173.

Chen, C. C. J., Spanò, G., & Edgin, J. O. (2013). The impact of sleep disruption on executive function in Down syndrome. *Research in developmental disabilities*, *34*(6), 2033-2039.

Chu, J., & Richdale, A. L. (2009). Sleep quality and psychological wellbeing in mothers of children with developmental disabilities. *Research in Developmental Disabilities*, *30*(6), 1512-1522.

Churchill, S. S., Kieckhefer, G. M., Landis, C. a., & Ward, T. M. (2011). Sleep measurement and monitoring in children with Down syndrome: A review of the literature, 1960–2010. *Sleep Medicine Reviews*, *16(5)*, 477–488.

Classification of Sleep Disorders (3rd ed.). Darien, IL.

Cohen, S., Fulcher, B. D., Rajaratnam, S. M., Conduit, R., Sullivan, J. P., St Hilaire, M. A., ... & Braga-Kenyon, P. (2018). Sleep patterns predictive of daytime challenging behavior in individuals with low-functioning autism. *Autism Research*, *11*(2), 391-403.

Comella, C. L. (2013). Treatment of Restless Legs Syndrome. *Neurotherapeutics, 11(1), 177–187*.doi:10.1007/s13311-013-0247-9

Conant, K. D., Thibert, R. L., & Thiele, E. A. (2009). Epilepsy and the sleep–wake patterns found in Angelman syndrome. *Epilepsia*, *50*(11), 2497-2500.

Dagli, A. I., Mueller, J., & Williams, C. A. (2017). Angelman syndrome. In *GeneReviews®[Internet]*. University of Washington, Seattle.

De Leersnyder, H., de Blois, M. C., Claustrat, B., Romana, S., Albrecht, U., von Kleist-Retzow, J. C., ... & Munnich, A. (2001). Inversion of the circadian rhythm of melatonin in the Smith-Magenis syndrome. *The Journal of pediatrics*, *139*(1), 111-116.

Edelman, E. A., Girirajan, S., Finucane, B., Patel, P. I., Lupski, J. R., Smith, A. C. M., & Elsea, S. H. (2007). Gender, genotype, and phenotype differences in Smith–Magenis syndrome: a meta-analysis of 105 cases. *Clinical genetics*, *71*(6), 540-550.

Emerson, E., Felce, D., & Stancliffe, R. J. (2013). Issues concerning self-report data and population-based data sets involving people with intellectual disabilities. *Intellectual and developmental disabilities*, *51*(5), 333-348.

Falco, M., Amabile, S., & Acquaviva, F. (2017). RAI1 gene mutations: mechanisms of Smith–Magenis syndrome. *The application of clinical genetics*, *10*, 85-94.

Fallone, G., Acebo, C., Seifer, R., & Carskadon, M. A. (2005). Experimental restriction of sleep opportunity in children: effects on teacher ratings. *SLEEP 28*(12), 1561-1567.

Fallone, G., Owens, J. A., & Deane, J. (2002). Sleepiness in children and adolescents: clinical implications. *Sleep medicine reviews*, *6*(4), 287-306.

Foley, D. C., & McCutcheon, H. (2004). Detecting pain in people with an intellectual disability. *Accident and Emergency Nursing*, *12*(4), 196-200.

Glassman, L. W., Grocott, O. R., Kunz, P. A., Larson, A. M., Zella, G., Ganguli, K., & Thibert, R. L. (2017). Prevalence of gastrointestinal symptoms in Angelman syndrome. *American Journal of Medical Genetics Part A*, *173*(10), 2703-2709.

Gropman, A. L., Duncan, W. C., & Smith, A. C. (2006). Neurologic and developmental features of the Smith-Magenis syndrome (del 17p11. 2). *Pediatric neurology*, *34*(5), 337-350.

Horsler, K., & Oliver, C. (2006). The behavioural phenotype of Angelman syndrome. *Journal of Intellectual Disability Research*, *50*(1), 33-53.

Horvath, K., & Perman, J. A. (2002). Autism and gastrointestinal symptoms. *Current gastroenterology reports*, *4*(3), 251-258.

Hyman, P., Oliver, C., & Hall, S. (2002). Self-injurious behavior, self-restraint, and compulsive behaviors in Cornelia de Lange syndrome. *American Journal on Mental Retardation*, *107*(2), 146-154.

Jan, J. E., Owens, J. A., Weiss, M. D., Johnson, K. P., Wasdell, M. B., Freeman, R. D., & Ipsiroglu, O. S. (2008). Sleep hygiene for children with neurodevelopmental disabilities. *Pediatrics*, *122*(6), 1343-1350.

Kim, B. R., Stifter, C. A., Philbrook, L. E., & Teti, D. M. (2014). Infant emotion regulation: Relations to bedtime emotional availability, attachment security, and temperament. *Infant Behavior and Development*, *37*(4), 480-490.

Krakowiak, P., Goodlin-Jones, B., Hertz- Picciotto, I. R. V. A., Croen, L. A., & Hansen, R. L. (2008). Sleep problems in children with autism spectrum disorders, developmental delays, and typical development: a population- based study. *Journal of sleep research*, *17*(2), 197-206.

Long, A. C., Krishnamurthy, V., & Palermo, T. M. (2007). Sleep disturbances in school-age children with chronic pain. *Journal of pediatric psychology*, *33*(3), 258-268.

Mannion, A., Leader, G., & Healy, O. (2013). An investigation of comorbid psychological disorders, sleep problems, gastrointestinal symptoms and epilepsy in children and adolescents with autism spectrum disorder. *Research in Autism Spectrum Disorders*, *7*(1), 35-42.

Martin, N., Oliver, C., & Hall, S. (2000). Obswin, Version 3.0. Birmingham: University of Birmingham.

McGuire, B. E., Daly, P., & Smyth, F. (2010). Chronic pain in people with an intellectual disability: under-recognised and under-treated?. *Journal of Intellectual Disability Research*, *54*(3), 240-245.

Medicine, A. A. o. S. (2014). *American Academy of Sleep Medicine International*

Merkel, S. I., Voepel-Lewis, T., Shayevitz, J. R., & Malviya, S. (1997). The FLACC: a behavioral scale for scoring postoperative pain in young children. *Pediatric nursing*, *23*(3), 293-298.

Miano, S., Bruni, O., Elia, M., Musumeci, S.A., Verillo, E., & Ferri, R. (2005). Sleep breathing and periodic leg movement pattern in Angelman syndrome: A polysomnograpic study. *Clinical Neurophysiology*, *116*, 2685-2692.

Moss, J., Oliver, C., Hall, S., Arron, K., Sloneem, J., & Petty, J. (2005), The association between environmental events and self- injurious behaviour in Cornelia de Lange syndrome. *Journal of Intellectual Disability Research*, *49*, 269-277. doi:10.1111/j.1365-2788.2005.00649.x

Nation, J., & Brigger, M. (2017). The efficacy of adenotonsillectomy for obstructive sleep apnea in children with Down syndrome: a systematic review. *Otolaryngology–Head and Neck Surgery*, *157*(3), 401-408.

Oliver, C., Horsler, K., Berg, K., Bellamy, G., Dick, K., & Griffiths, E. (2007). Genomic imprinting and the expression of affect in Angelman syndrome: what's in the smile?. *Journal of Child Psychology and Psychiatry*, *48*(6), 571-579.

Paprocka, J., Kijonka, M., Wojcieszek, P., Pęcka, M., Emich-Widera, E., & Sokół, M. (2017). Melatonin and Angelman syndrome: implications and mathematical model of diurnal secretion. *International journal of endocrinology*, *2017*.

Pelc, K., Cheron, G., Boyd, S. G., & Dan, B. (2008). Are there distinctive sleep problems in Angelman syndrome?. *Sleep medicine*, *9*(4), 434-441.

Picchietti, M. A., & Picchietti, D. L. (2008). Restless Legs Syndrome and Periodic Limb Movement Disorder in Children and Adolescents. *Seminars in Pediatric Neurology, 15(2), 91–99.*doi:10.1016/j.spen.2008.03.005

Potocki, L., Glaze, D., Tan, D. X., Park, S. S., Kashork, C. D., Shaffer, L. G., ... & Lupski, J. R. (2000). Circadian rhythm abnormalities of melatonin in Smith-Magenis syndrome. *Journal of medical genetics*, *37*(6), 428-433.

Richdale, A., Francis, A., Gavidia-Payne, S., & Cotton, S. (2000). Stress, behaviour, and sleep problems in children with an intellectual disability. *Journal of Intellectual and Developmental Disability*, *25*(2), 147-161.

Rzepecka, H., McKenzie, K., McClure, I., & Murphy, S. (2011). Sleep, anxiety and challenging behaviour in children with intellectual disability and/or autism spectrum disorder. *Research in Developmental Disabilities*, *32*(6), 2758-2766.

Schwichtenberg, A. J., Choe, J., Kellerman, A., Abel, E. A., & Delp, E. J. (2018). Pediatric Videosomnography: Can Signal/Video Processing Distinguish Sleep and Wake States?. *Frontiers in pediatrics*, *6*, 158. doi:10.3389/fped.2018.00158

Short, M. A., Gradisar, M., Lack, L. C., Wright, H. R., & Chatburn, A. (2013). Estimating adolescent sleep patterns: parent reports versus adolescent self-report surveys, sleep diaries, and actigraphy. *Nature and science of sleep*, *5*, 23-26.

Smith, A. C., Dykens, E., & Greenberg, F. (1998). Behavioral phenotype of Smith-Magenis syndrome (del 17p11. 2). *American journal of medical genetics*, *81*(2), 179-185.

Stickgold, R. (2005). Sleep-dependent memory consolidation. Nature, 437(7063), 1272.

Surtees, A. D., Oliver, C., Jones, C. A., Evans, D. L., & Richards, C. (2018). Sleep duration and sleep quality in people with and without intellectual disability: a meta-analysis. *Sleep medicine reviews*, *40*, 135-150.

Takaesu, Y., Komada, Y., & Inoue, Y. (2012). Melatonin profile and its relation to circadian rhythm sleep disorders in Angelman syndrome patients. *Sleep medicine*, *13*(9), 1164-1170.

Teti, D. M., Kim, B. R., Mayer, G., & Countermine, M. (2010). Maternal emotional availability at bedtime predicts infant sleep quality. *Journal of Family Psychology*, *24*(3), 307.

Tietze, A. L., Blankenburg, M., Hechler, T., Michel, E., Koh, M., Schlüter, B., & Zernikow, B. (2012). Sleep disturbances in children with multiple disabilities. *Sleep medicine reviews*, *16*(2), 117-127.

Trickett, J., Heald, M., Oliver, C., & Richards, C. (2018). A cross-syndrome cohort comparison of sleep disturbance in children with Smith-Magenis syndrome, Angelman syndrome, autism spectrum disorder and tuberous sclerosis complex. *Journal of neurodevelopmental disorders*, *10*(1), 9. doi:10.1186/s11689-018-9226-0

Trickett J., Heald, M., Surtees, A., Clarkson, E., Agar, G., Oliver, C., & Richards, C. (2017). Actigraphy Cleaning Protocol. University of Birmingham, Birmingham.

Trickett, J., Oliver, C., Heald, M., Denyer, H., Surtees, A., Clarkson, E., ... & Richards, C. (2019a). Sleep in children with Smith–Magenis syndrome: a case–control actigraphy study. *Sleep* doi 10.1093/sleep/zsz260

Trickett, J., Oliver, C., Heald, M., Denyer, H., Surtees, A., Clarkson, E., ... & Richards, C. (2019). Multi-method assessment of sleep in children with Angelman syndrome: A case-controlled study. *Frontiers in Psychiatry, 10*, 874.

Van De Water, A. T., Holmes, A., & Hurley, D. A. (2011). Objective measurements of sleep for non-laboratory settings as alternatives to polysomnography–a systematic review. *Journal of sleep research*, *20*(1pt2), 183-200.

Vriend, J., & Corkum, P. (2011). Clinical management of behavioral insomnia of childhood. *Psychology research and behavior management*, *4*, 69-79.

Waite, J., Heald, M., Wilde, L., Woodcock, K., Welham, A., Adams, D., & Oliver, C. (2014). The importance of understanding the behavioural phenotypes of genetic syndromes associated with intellectual disability. *Paediatrics and Child Health, 24(10), 468–472.* doi:10.1016/j.paed.2014.05.002

Wiggs, L., & France, K. (2000). Behavioural treatments for sleep problems in children and adolescents with physical illness, psychological problems or intellectual disabilities. *Sleep Medicine Reviews*, *4*(3), 299-314.

Wilde, L., Silva, D., & Oliver, C. (2013). The nature of social preference and interactions in Smith–Magenis syndrome. *Research in developmental disabilities*, *34*(12), 4355-4365.