Title: Choice making in Rett syndrome: A descriptive study using video data

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Implications for Rehabilitation

- The provision of adequate time allowing for a response will promote effective choice making in girls and women with Rett syndrome
- Although almost all girls and women with Rett syndrome used eye gaze to indicate their choice, communication partners also need to recognise and respond to other communication modalities that are sometimes used like body movements

Choice making in Rett syndrome: A descriptive study using video data

Abstract

Purpose: To describe the choice making abilities of girls and women with Rett syndrome.

Method: Females with Rett syndrome registered with the Australian Rett Syndrome Database with a pathogenic *MECP2* mutation were included in this study. Video clips showing choice making in 64 females at a median age of 11.6 years (range 2.3 – 35.6 years) were analysed. Video clips were coded for the location and nature of the choice making interaction, and the actions of the communication partner and female with Rett syndrome.

Results: The majority (82.8%, 53/64) of females made a choice, most using eye gaze. Just under half (24/53) used one modality to communicate their choice, 52.8% used two modalities and one used three modalities. Of those who made a choice, 50% did so within 8 seconds. The length of time to make a choice did not appear to vary with age. During choice making, 57.8% (37/64) of communication partners used language and gestures, 39.1% (25/64) used only language and two used language, gestures and symbols within the interaction.

Conclusions: The provision of adequate time allowing for a response and observation for the use of multiple modalities could promote effective choice making in females with Rett syndrome.

Introduction

Rett syndrome is a neurodevelopmental disorder caused by mutations in the X-linked *MECP2* gene and seen mainly in females [1]. Development in Rett syndrome appears to be largely typical prior to the occurrence of a period of regression during which hand stereotypies develop and impaired language and motor abilities become apparent. These impairments are often severe and remain present to varying degrees throughout the lifespan [2].

The majority of females with Rett syndrome experience difficulties with communication, [3-5] and only small proportions use words [6] or gestures for communication [4]. More commonly, affected females use eye gaze [4,7] which has been recognised as a communicative strength of girls and women with Rett syndrome since the early 1990s [8] and is considered a supportive feature for a diagnosis [2,9]. Body movements and communication devices including picture boards are also used by some females for communication [7].

Providing females with Rett syndrome with opportunities to communicate their needs and desires has the potential to positively influence their participation in everyday life [10]. Therefore is it not surprising that choice making has been described as the most commonly targeted communicative function by speech language pathologists working with individuals with Rett syndrome [11] and the most common reason for using eye gaze technology with individuals with Rett syndrome [12]. Two UK studies, one using multidisciplinary clinical assessment [3] and the other a questionnaire completed by caregivers [13] , reported that 51.2% (43/84) and 67.0% (61/91) of females with Rett syndrome were able to make a choice, respectively. Studies with smaller sample sizes provide some further insight into choice making abilities. Results from a study that specifically assessed choice making in seven girls [14] as well as those from our own interview study with 17 parents [5] demonstrated that females with Rett syndrome had the ability to make a choice, even if they did not do this consistently

[5,14]. Girls and women with Rett syndrome may also be able to learn to make choices using augmentative and alternative communication methods according to small sample studies involving three [15] , four [16] and seven females [17].

Despite the importance of choice making, the current literature does not provide a detailed description of choice making abilities of girls and women with Rett syndrome. Nor does the literature adequately describe the relationships between choice making and factors known to influence other communication abilities such as *MECP2* mutation type [6] and the context of the communicative interaction [18,19]. We therefore conducted this study to describe the choice making abilities of girls and women with Rett syndrome and the factors that may influence their ability to make a choice using video data available in the Australian Rett syndrome Database (ARSD) [20].

Methods

Participants

Participants for this study were sampled from the population-based Australian Rett Syndrome Database (ARSD), established in 1993. The ARSD uses a variety of methods, including video, to collect longitudinal data on Australian girls and women with Rett syndrome born since 1976 [20]. Upon enrolment into the database, families complete an initial questionnaire about the early development, regression period and current functioning of the girl or woman with Rett syndrome. This questionnaire includes questions about speech-language abilities [6]. Additionally, since the year 2000 families have completed a follow-up questionnaire approximately every two years. This questionnaire includes questions about medical conditions and care, specific Rett syndrome behaviours, the use of resources such as therapy and everyday functioning including walking ability.

In 2004, 2007 and 2012 families registered with the database were invited to provide information on their daughter's functional abilities, using two tools: a video based filming protocol and a parent-

report questionnaire [20]. The filming protocol was broadly based on the domains of the Functional Independence Measure for Children (WeeFIM) [21] and asked parents to film their daughter performing a range of functional tasks, including a choice-making activity [20]. Video clips of choice-making of girls and women with a pathogenic *MECP2* mutation were included in this study.

Procedure

The video based filming protocol instructed parents/caregivers to show the girl/woman with Rett syndrome two objects, such as two items of food, and ask her to indicate her preference. Videos of choice making interactions were included if the girl/woman was instructed by a communication partner to make a choice between two or more different items and that the items and the girl/woman were visible for the duration of the interaction. The video also needed to be of satisfactory quality so the interaction could be clearly seen and heard. If a girl or woman had more than one video meeting the inclusion criteria (i.e. a video had been provided in multiple years), each video was coded and the one demonstrating their best ability to make a choice was included in this study. Videos where the girl/woman made a choice were included in favour of videos where she did not, and videos with a faster time to choice were included in preference to those with a slower time to choice.

In total, 372 videos across the three time points were available for 215 girls and women. Of these videos, 179 included a choice making interaction for 122 girls and women and 78 videos met the inclusion criteria for the choice making interaction as outlined above. Fourteen videos were excluded from analysis as the parent/caregiver had provided another video of a choice making interaction representing better abilities. Therefore 64 videos of choice making interactions, representing 64 females with Rett syndrome, were analysed in this study (figure 1).

Insert figure 1 about here

- *Video coding*

A coding framework was developed specifically for the purpose of this study that identified: the location of the interaction, for example at the participant's home; who the communication partner was, for example a parent or a staff member; the number and description of choice items; the physical position of the girl/woman with Rett syndrome and whether the girl/woman made a choice. The communication modalities used by the communication partner and the girl/woman with Rett syndrome were coded into categories based on The Communication Matrix [22], an evidence-based assessment tool of expressive communication of people with severe and multiple disabilities [23]. This included coding information about eye gaze and whether the girl or woman looked at the item and back at the communication partner. A choice indicated with eye gaze was coded if the individual looked at an item longer than another.

Initially the ability to make a choice was coded into one of three categories; able to make an independent choice, able to make a choice with prompts and not able to make a choice. If the girl or woman indicated her choice following the communication partner's initial instruction without any repeat of instruction or additional prompts such as pointing to the items, she was coded as making an independent choice. If the girl or woman indicated her choice after a repeat of the instruction or after the communication partner used prompts they were coded as making a choice with prompts.

The coding framework was piloted by the first two authors with nine videos. There was a high level of agreement in relation to the majority of elements of the coding framework however the definition of the choice making outcome was changed from three categories, as described above, to two categories; choice and no choice. The modification was made as some communication partners used prompts when they presented the choice making scenario, such as pointing at the choice items as they labelled them, therefore the distinction between the ability to make an independent choice and a choice with prompts was not clear.

All videos were coded according to the outlined framework by the first author. The coding included recording verbal and nonverbal forms of communication used by the girl/woman or communication

partners. The length of time taken to make a choice (seconds) was also determined by measuring the time between the communication partner ending the first verbal instruction and the girl/woman indicating her choice.

- *Inter-Rater Reliability*

The first two authors coded 15 videos to determine whether or not a choice was made. The inter-rater reliability for coding whether or not a choice was made between the first and second author were calculated using Cohen's Kappa statistic [24]. A kappa coefficient above 0.8 was interpreted as excellent, 0.6 – 0.8 as substantial, 0.4 – 0.6 as moderate and below 0.4 as poor [25]. The kappa coefficient was 0.7 (95% CI 0.19 – 1.15) indicating substantial reliability.

Other variables

Age was calculated at the time the video was returned to the ARSD and categorised into the following groups; < 8 years, 8 < 13 years, 13 < 19 years and ≥ 19 years representing the preschool and early school years, primary school years, adolescence and adulthood. The type of *MECP2* mutation was coded as one of the following: early truncation, large deletion, C-terminal deletion, p.Arg106Trp, p.Arg133Cys, p.Arg168*, p.Arg255*, p.Arg270*, p.Arg294*, p.Arg306Cys, p.Thr158Met or a group of other miscellaneous mutations. The ability to walk and to grasp objects was coded using video data from the same time point as the choice making interaction. The ability to walk was coded in one of the following three categories: able to walk 10 steps independently, able to walk 10 steps with minimal or moderate assistance, or able to walk 10 steps with maximal assistance or unable to walk [26]. The ability to grasp objects was coded in a binary fashion; independent if the girl/woman was able to grasp and pick up an object of any size; and unable to grasp if they required assistance or were not able to grasp [27]. Using follow-up questionnaire data, we also measured walking abilities over time using up to six observation points. In each follow-up questionnaire walking was categorised as walking

independently, able to walk with assistance or unable to walk. Using using latent class group analysis a trend indicator that described the trajectory of walking was created and resulted in four distinct groups 1) always walked independently; 2) always walked with assistance; 3) deteriorating walking abilities and 4) always was unable to walk [28]. Data on babbling and saying words at enrolment into the ARSD was obtained from responses to the question, "Which of the following best describes your child's use of speech at the present? No speech, babble, single words, 2 word sentences, 3 word sentences or 4 or more word sentences" in the initial questionnaire completed by families.

Data analysis

Chi squared and Fisher's exact test was used to compare the proportions of different *MECP2* mutation types and walking trajectory of our sample to that of individuals registered with the ARSD but not in our study. Descriptive statistics were used to describe the characteristics of our sample and their choice making interactions. Fisher's exact test was also used to compare the proportion able to make a choice or not by age group, type of *MECP2* mutation, the ability to walk and grasp objects, and speech-language ability at enrolment into the ARSD. The Kaplan-Meier method was used to estimate the probability of making a choice, overall and by age group. The log-rank test was used to test the homogeneity of time-to-event functions across strata. All analyses were conducted using STATA 12 [29].

Results

At the time of the video, the 64 females were aged 2.30 – 35.64 years with a median age of 11.65 years. The most common mutation in our sample was p.Arg270* (14.06%, 9/64) and p.ThrT158Met (11.44%, 27/236) was the most common mutation in those in the ARSD not include in our study (table 1). Overtime, 46.03% (29/63) of girls/women in our sample always walked independently in comparison to 34.27% (73/213) of girls/women in the ARSD not included in our study. The proportions

of different *MECP2* mutation types (n=64) and walking trajectories (n=63) in our sample did not differ significantly from the proportion of different *MECP2* mutation types (n=236, p=0.43) and walking trajectories (n=213, p=0.24) in the ARSD who were not included in our study.

Insert table 1 about here

The characteristics of the sample and their ability to make a choice are presented in table 2. The majority (82.81%, 53/64) of our sample made a choice between two or more items. For those who made a choice (n=53) the length in time it took to make a choice ranged from 1 second to 4 minutes 6 seconds with a mean of 14.47 (SD 33.57) seconds. Females of different age groups, *MECP2* mutation types, walking and grasping ability and speech-language ability at enrolment into the ARSD were able to make a choice. The proportion able to make a choice did not appear to vary according to age group, *MECP2* mutation type, the ability to walk or grasp or speech language ability at enrolment into the ARSD (table 2).

Insert table 2 about here

Videos were filmed at home for 71.87% (46/64) of the sample, at school for 21.87% (14/64), at group homes for 4.69% (3/64) and one individual was filmed at her day centre. Most (87.50%, 56/64) girls/women were sitting during the video, 7.81% (5/64) were standing, 3.13% (2/64) were taking steps and one alternated between standing still and taking steps. The mother of the female with Rett syndrome was the communication partner in most (67.19%, 43/64) videos and the father of the girl/woman was the communication partner in 4.69% (3/64). The remaining videos involved other communication partners who were school, group home or day centre staff members. Most (73.44%, 47/64) videos were filmed by another person that was not the communication partner.

The females with Rett syndrome were most often asked to make a choice between different foods (42.18%, 27/64) or different movies (29.69%, 19/64). Other interactions involved making a choice between different drinks, toys and activities. All communication partners used language with 57.8%

(37/64) also using gestures and two using a combination of language, gestures and symbols. All, except one who used photos, asked the female with Rett syndrome to make a choice between concrete objects. The majority of females (93.75%, 60/64) were asked to make a choice between two items; three were asked to make a choice between three items and two did this successfully and one was asked to make a choice between four items and achieved this successfully.

Of those who communicated their choice, almost all (51/53) looked at the item to indicate their choice (table 3). Of these, seven first looked at their choice and then back at the communication partner. Just under half (24/53) used one modality to communicate their choice, slightly more than half (28/53) used two modalities and one females used three modalities. Figure 2 illustrates, of the 53 females who made a choice, 25% did so by 5 seconds, 50% by 8 seconds and 75% by 22 seconds. Three quarters of females aged 8 to 13 years demonstrated choice making compared with 93% of females aged 13 to 19 years. The median speed of choice making was fastest for those younger than 8 years (p=0.08) (figure 3).

Insert table 3 about here

Insert figure 2 and 3 about here

The girls and women who did not make a choice (17.19%, 11/64) fell into two groups; 1) those who did not appear to acknowledge the items presented, as demonstrated by not looking at the items at any point during the interaction (54.55%, 6/11), and 2) those who looked at the items but made no clear indication as to which one was their choice (45.45%, 5/11). An example of a female from the first group was a girl who was asked to make a choice between a glass of cola and water, the girl did not look at either item and maintained her eye gaze away from the items. An example of someone in the second group was a girl who moved between looking at each item and around the room, without spending more time looking at one item more than the other or using another modality to indicate a choice.

Discussion

This study described the choice making abilities of girls and women with Rett syndrome by observing video data collected in everyday settings. The majority of our sample seemed to be able to make a choice, in contrast to previous studies that reported between half and two thirds of girls and women with Rett syndrome were able to make choices [3,13]. We analysed video data of girls and women in familiar environments with familiar communication partners, factors which may positively influence communicative interactions with girls and women with Rett syndrome [7,18,19]. This might explain the higher proportion of girls and women able to make a choice in our study in comparison to previous research using multidisciplinary clinical assessment [3] or caregiver questionnaire [13]. While the majority in our study made a choice, the time needed to make a choice varied greatly. Time taken to make a choice has not been previously documented in Rett syndrome, although varied response times to a stimulus in general have been reported [7]. Nevertheless, those who did not make a choice in our study may have not been given enough time to make a choice [7] or sufficiently motivated by the items presented [14,17].

Approximately half of our sample used a combination of modalities to communicate their choice, of which eye gaze was most frequently used. This provides further evidence for eye gaze as a communicative strength of girls and women with Rett syndrome [4,7,8]. It also validates parent report data on 16 girls and women with Rett syndrome where of the multiple modalities used to communicate, eye gaze was most commonly used for choice making [5]. Among those who used eye gaze in our study, seven demonstrated some joint attention by looking at the item and then back at the communication partner [30]. This indicates that some females with Rett syndrome may have more advanced eye gaze abilities than others as previously identified in a larger study of females from the ARSD using parent report Communication and Symbolic Behavior Scales Developmental Profile Infant-Toddler Checklist [31] data [32]. Families and professionals supporting girls and women with Rett syndrome need to be aware of the multiple modalities that may be used to make a choice but that

eye gaze appears to be a preference and may therefore be a good target for intervention. Future research protocols need to take the multiple modalities into consideration and not limit choice making definitions to a specific modality.

In our study, the capacity to make a choice did not vary according to age, *MECP2* mutation type, walking ability or hand function, and the time taken to make a choice did not vary according to age group. However the lack of apparent relationships between these factors and the capacity to make a choice and the time taken to make a choice may be due to poor statistical power as a result of our small sample size. Other factors not included in our study, such as the type of reinforcement provided by communication partners [17] and the presence and severity of dyspraxia [7], may influence whether or not a girl or woman with Rett syndrome is able to make choices and how quickly the choice is made. Relationships between the communication modalities used by the female with Rett syndrome to make a choice and factors such as *MECP2* mutation type and walking or grasping abilities were not analysed in this study. Nevertheless it is likely that genotype impacts on the type of modalities used as those with the p.Arg133Cys mutation are likely to have a greater use of words [6]. Moreover girls and women with greater functional abilities, such as hand use and mobility may have access to a greater repertoire of communication modalities [5]. Future research using valid and reliable methods to look at the consistency of choice making over time in different contexts and with different communication partners is needed.

Previous research in Rett syndrome has not detailed the specific communication modalities used by communication partners in their interactions with girls and women with Rett syndrome. We found all communication partners used language in their interactions, over half combined language with gestures and two combined language with gestures and symbols. This is not surprising given parents/caregivers were instructed to ask the females to indicate her choice. Only two communication partners used symbols in their interactions even though the use of communication aids, including pictures of items, commonly makes choice making occur more often and clearly as reported by speech

language pathologists working with girls and women with Rett syndrome [11]. It would be interesting to investigate how the communication modalities used by communication partners impact the success of choice making and other important communicative functions to inform future communication interventions.

This is the largest descriptive study to date using video data to demonstrate the choice making abilities of girls and women with Rett syndrome. As a result we have been able to contribute unique information to the existing literature. Nevertheless a number of limitations need to be taken into consideration when interpreting our results. Our study described the ability of the girl or women to make a choice at one point in time and therefore may not represent her usual abilities. Although using a naturalistic context with familiar communication partners to elicit choice making abilities has its strengths, it also means the sampling context was not standardised across participants and this limits comparisons between participants. This also means the way in which the choice was presented varied across interactions which may have impacted in the individual's ability to make a choice and we were unable to test the validity of the participants' choice making [33]. Additionally, caregivers were not instructed to wait for a minimum amount of time following their instruction therefore girls and women who did not make a choice may have been able to do so if given more time. Although our coding framework was developed based on a review of the literature and piloted, the researcher may have not coded a choice that parents/caregivers or other familiar communication partners usually respond to [34]. Finally, although our study is the largest of its kind, we still had limited statistical power when analysing relationships between choice making and factors such as *MECP2* mutation type and it is not known if the girls and women excluded from this study were able to make a choice.

We found the majority of girls and women with Rett syndrome can make choices in naturalistic contexts with familiar communication partners. Half of our sample made a choice within eight seconds although one female required four minutes and six seconds to make her choice. Eye gaze was frequently used to communicate choices, sometimes in combination with other communications

modalities such as body movements and gestures, and communication partners always used language, sometimes in combination with gestures or symbols. Although we did not find a relationship between age, *MECP2* mutation type and level of functional abilities and the ability to make a choice, it is still likely these factors may influence the types of modalities used to communicate a choice. Our findings provide further evidence to support the use of communication strategies some families and professionals are already using including observing for the use of multiple modalities and waiting for a response [5,11] but clarify the length of waiting time that may be required.

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Declarations of Interest

The authors report no declarations of interest.

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Table 1. Proportion of *MECP2* mutation types and walking trajectories of our sample (n=64) and those in the ARSD not included in this study (n=236).

Characteristic	Our sample n (%)	Those in the ARSD not included in this study n (%)	*p*-value[a]
Mutation type			
p.Arg106Trp	3 (4.69%)	11 (4.66%)	
p.Arg133Cys	6 (9.38%)	17 (7.20%)	
p.Arg168*	6 (9.38%)	26 (11.02%)	
p.Arg255*	6 (9.38%	11 (4.66%)	
p.Arg270*	9 (14.06%)	19 (8.05%)	
p.Arg294*	6 (9.38%)	18 (7.63%)	
p.Arg306Cys	5 (7.81%)	13 (5.51%)	
p.Thr158Met	4 (6.25%)	27 (11.44%)	
C-terminal deletion	6 (9.38%)	22 (9.32%)	
Early truncation	1 (1.56%)	22 (9.32%)	
Large deletion	4 (6.25%)	18 (7.63%)	
Other	8 (12.50%)	32 (13.56%)	0.43
Walking trajectory[b]			
Always walked independently	29 (46.03%)	73 (34.27%)	
Always walked with assistance	8 (12.70%)	33 (15.49%)	
Deteriorating walking abilities	11 (17.46%)	32 (15.02%)	
Always unable to walk	15 (23.81%)	75 (35.21%)	0.24

[a] Fisher's exact test was used to compare the proportion of mutation types between groups and chi square was used to compare the proportion of walking trajectory categories

[b] Walking trajectory data available for 63/64 cases in our sample and for 213/236 cases in the ARSD not included in this study

Table 2. Proportion able to make a choice by sample characteristics.

Characteristic (n)	Able to make a choice n (%)		*p*-value[a]
	Yes	No	
Age group (64)			
≤ 8 years (16)	14 (87.50%)	2 (12.50%)	
8 < 13 years (20)	15 (75.00%)	5 (25.00%)	
13 < 19 years (14)	13 (92.86%)	1 (7.14%)	
≥ 19 years (14)	11 (78.57%)	3 (21.43%)	0.54
Mutation type (64)			
p.Arg106Trp (3)	3 (100.00%)	0	
p.Arg133Cys (6)	5 (83.33%)	1 (16.67%)	
p.Arg168* (6)	5 (83.33%)	1 (16.67%)	
p.Arg255* (6)	4 (66.67%)	2 (33.33%)	
p.Arg270* (9)	7 (77.78%)	2 (22.22%)	
p.Arg294* (6)	5 (83.33%)	1 (16.67%)	
p.Arg306Cys (5)	4 (80.00%)	1 (20.00%)	
p.Thr158Met (4)	4 (100.00%)	0	
C-terminal deletion (6)	5 (83.33%)	1 (16.67%)	
Early truncation (1)	1 (100.00%)	0	
Large deletion (4)	3 (75.00%)	1 (25.00%)	
Other (8)	7 (87.50%)	1 (12.50%)	1.00
Ability to walk (62)			
Independent (32)	26 (81.25%)	6 (18.75%)	
Minimal or Moderate Assistance (13)	11 (84.61%)	2 (15.38%)	
Maximal assistance or unable to walk (17)	14 (82.35%)	3 (17.65%)	1.00
Ability to grasp (58)			
Independent (33)	28 (84.85%)	5 (15.15%)	
Unable to grasp (25)	21 (84.00%)	4 (16.00%)	1.00
Speech-language ability at enrolment into the ARSD[b] (64)			
One or more words (12)	9 (75.00%)	3 (25.00%)	
Babble (33)	29 (87.88%)	4 (12.12%)	
No speech (19)	15 (78.95%)	4 (21.05%)	0.50

[a] *p*-value obtained using Fisher's exact test comparing the proportion of girls/women able to make a choice and different characteristics

[b] Data obtained from parent/caregiver completed questionnaire

Table 3. The frequency of different communication modalities girls and women with Rett syndrome used to make a choice.

Modality	Frequency[a]
Eye gaze	51
Body movements	
Takes item	7
Leans towards item	4
Gestures	
Gives item to communication partner	1
Points at item	2
Touches item without taking	7
Early sounds	2
Language	2

[a] The frequency will not equal the number of the girls/women who made a choice (n=53) as some girls and women used multiple modalities to indicate their choice

Figure captions

Figure 1. Flow chart of the selection of videos inclusion.

Figure 2. Kaplan-Meier survival curve for the ability to make a choice by time (n=53).

Figure 3. Kaplan-Meier survival curve for the ability to make a choice at different ages, by time (n=53).

Figure 1

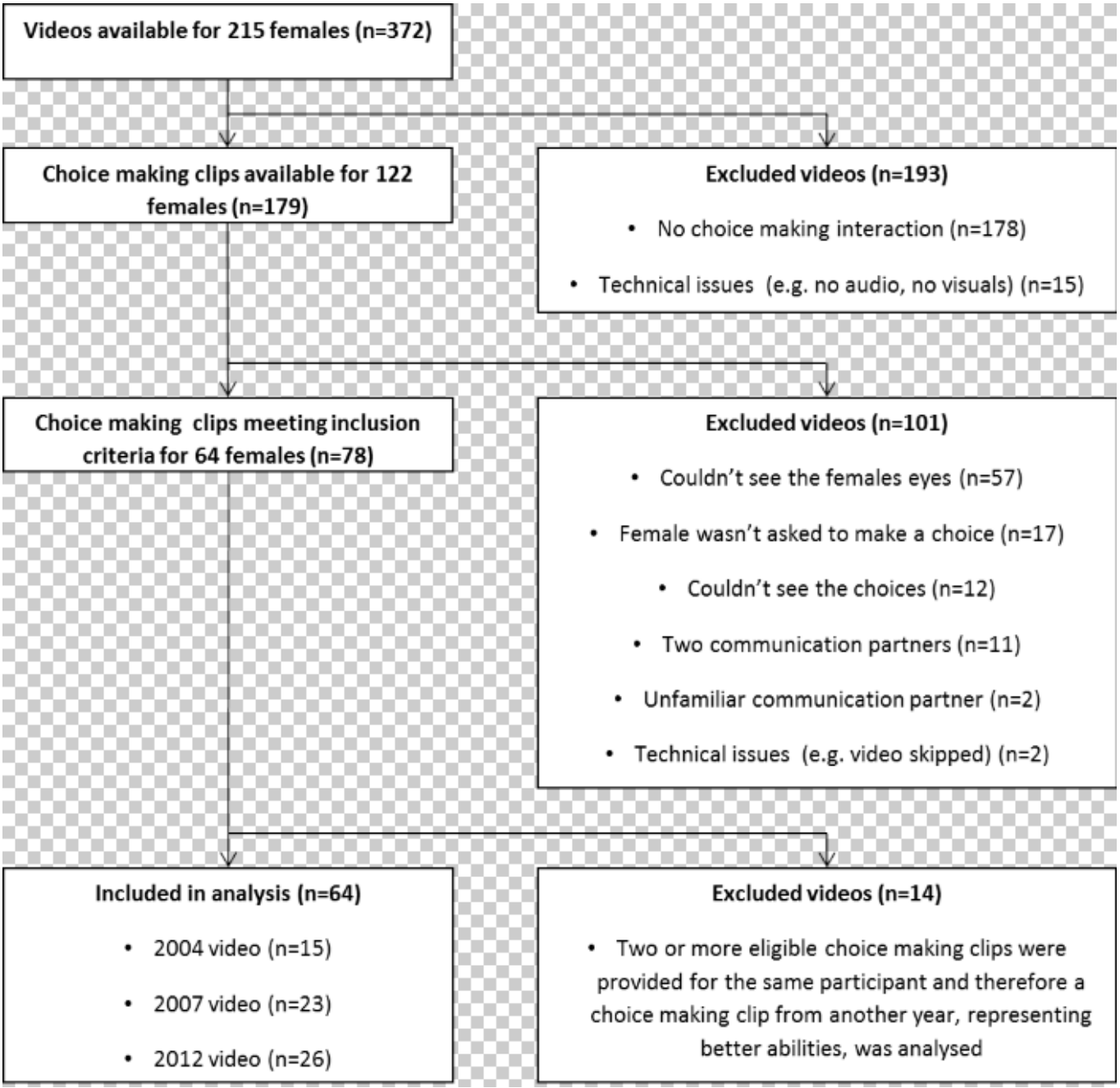
Videos available for 215 females (n=372)
Choice making clips available for 122 females (n=179)
Excluded videos (n=193)
• No choice making interaction (n=178)
• Technical issues (e.g. no audio, no visuals) (n=15)
Choice making clips meeting inclusion criteria for 64 females (n=78)
Excluded videos (n=101)
• Couldn't see the females eyes (n=57)
• Female wasn't asked to make a choice (n=17)
• Couldn't see the choices (n=12)
• Two communication partners (n=11)
• Unfamiliar communication partner (n=2)
• Technical issues (e.g. video skipped) (n=2)
Included in analysis (n=64)
• 2004 video (n=15)
• 2007 video (n=23)
• 2012 video (n=26)
Excluded videos (n=14)
• Two or more eligible choice making clips were provided for the same participant and therefore a choice making clip from another year, representing better abilities, was analysed

Figure 2

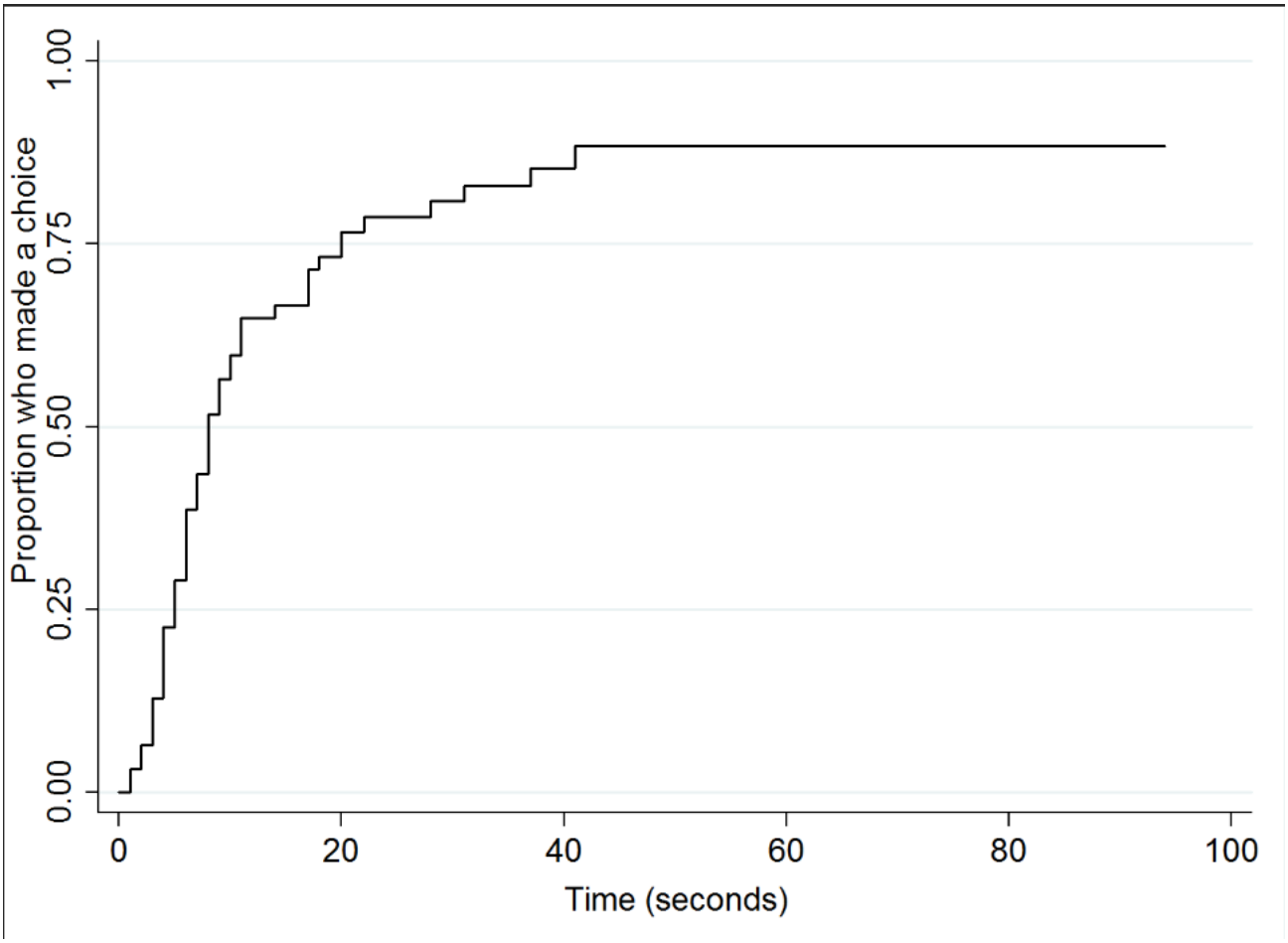

Figure 3