Identifying characteristics of non-completers in fear conditioning paradigms with children and adolescents

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Abstract
The number of studies on fear conditioning in children and adolescents has increased in recent years. Most of these studies exclusively focus on data of completers while dropout rates, reasons for dropout, and specific characteristics of non-completers are underreported. This study systematically investigated data of 283 children and adolescents between 8 and 17 years (M = 11.10, SD = 2.14) undergoing a differential fear conditioning paradigm using a female scream as unconditioned stimulus (US). The sample included 230 children and adolescents with a current primary anxiety disorder (separation anxiety disorder, social anxiety disorder, and specific phobia) and 53 non-anxious controls. The dropout rate was 24.1%. The most common reason to discontinue was being afraid of the US (59.1%) followed by the startle probe being too loud (15.2%). Logistic regressions revealed that younger age and a present anxiety disorder predicted dropout. There seem to be distinct characteristics potentially predicting dropout from fear conditioning paradigms. Thus, interpretability and generalizability of those paradigms are limited when non-completers are not considered. Future research should conscientiously look at these data more closely and investigate paradigms that work independent of age and diagnostic status.

Keywords
fear conditioning, extinction learning, anxiety disorder, non-completers, dropout

Introduction
Over the past years, a growing number of experimental studies on fear conditioning and extinction have been published targeting both clinical as well as developmental research questions in children and adolescents with and without an anxiety disorder (AD) (Dvir et al., 2019; Ryan et al., 2019). In general, during fear conditioning, a neutral stimulus is repeatedly paired with an aversive unconditioned stimulus (US), becoming a conditioned stimulus (CS+) that evokes fear independently of the US (conditioned response, CR). In differential fear conditioning, a second CS (CS-) is not paired with the US (Lonsdorf et al., 2017). Extinction subsequently describes the process in which the previously conditioned CS+ is now repeatedly presented without the US and a competing CS-no US association is created. In successful extinction, the CR to the CS+ is at best on par with the CR to the CS-.

In contrast to studies with adults, dropout rates are only reported occasionally in fear conditioning studies with children and adolescents, and if reported, the rates are often much higher than in adults (Den et al., 2015; Schiele et al., 2016; Shechner et al., 2015). Thus, studies mostly report exclusively the results of completers, potentially hampering interpretation and generalizability of the results of fear conditioning studies in children and adolescents. Indeed, in a recent review, Ryan et al. (2019) reported results of 35 studies investigating experimental parameters of extinction effects in differential fear conditioning in children and adolescents between 2 and 17 years. Only about half of the studies reported dropout rates with the number of non-completers varying between 10 and 50%. Taking a closer look at the studies reporting dropout rates, children discontinuing a fear conditioning paradigm tended to be younger (Britton et al., 2013) and more anxious than completers (Michalska et al., 2016). Regarding participants’ sex, studies yield mixed findings with Glenn et al. (2012) describing non-completers as more likely to be female, while Lau et al. (2008) identified that males are less likely to return for extinction. Looking at the specific reasons to discontinue, studies described the US as being too loud (Den et al., 2015), participants being afraid of the experimental stimuli in general (Glenn et al., 2012), or fearing the fear conditioning task itself (Jackson et al., 2017). In sum, the information provided in existing studies about dropout rates and reasons, as well as the description of non-completers of fear conditioning tasks seems to be rather inconsistent and often lacks information. Consequently, important information is lost and interpretability and generalizability of results is limited.

Ryan et al. (2019) refer to anxiety invoked by the experimental stimuli as a major reason for dropout. This is especially important, because fear conditioning and extinction are the mechanisms considered to be central in exposure-based treatments for ADs. Thus, systematic dropout may seriously distort the outcome of fear conditioning and extinction studies investigating anxiety treatment mechanisms in the laboratory. Again, existing results are inconsistent. Thus, it is necessary to further explore potential factors (e.g., age, sex, and individual evaluation of the experimental stimuli) that may increase the risk to discontinue fear conditioning paradigms in a large sample of children and adolescents. In addition, it is still unclear whether there are specific differences in dropout between AD subgroups. However, this might be relevant as, for example, children with separation anxiety or social anxiety disorder may be more likely to discontinue because the...
the participants (Treatment Center at the Ruhr University Bochum. Most of participants kept at the Mental Health Research and adolescents of two randomized control trials (RCTs) covering a wide age range (8–17 years) and various AD subgroups (specific phobia, social anxiety disorder, and separation anxiety disorder) as well as non-anxious controls. The wide age range as well as the different types of diagnoses allow us to conduct a comprehensive analysis of the characteristics of non-completers and, in contrast to previous research, render the possibility of group comparisons.

All analyses are conducted exploratory as they are based on data from two existing RCTs. In a first step, we evaluate the frequencies of dropout among children and adolescents and assess reasons named by the participants. In a second step, we aim at identifying the specific characteristics of children and adolescents who discontinue. Specifically, based on previous findings, we expect that dropout is associated with younger age, female gender, lower ratings of valence and higher ratings of arousal towards the US as well as anxiety symptoms and diagnostic status. In the last step, we investigate the unique association of every characteristic identified previously as possible predictor for dropout. To do so, we calculate a logistic regression model including the characteristics identified in the second step.

**Methods**

**Participants**

Participants ($N = 283$) were recruited via web-based advertisements and flyer, as well as from a database for participants kept at the Mental Health Research and Treatment Center at the Ruhr University Bochum. Most of the participants ($n = 230, 81.3\%$) were part of a multicenter RCT investigating the role of parental involvement in CBT (pre-registration: German CTR ID DRKS00009709) and participated in the paradigm as part of baseline measurements before therapy. The other participants were part of a non-clinical convenience sample investigating the role of a self-efficacy manipulation on extinction learning ($n = 53; 18.7\%$). Overall, participants ranged in age from 8 to 17 years ($M = 11.02, SD = 2.16$), and 55.8% ($n = 158$) were female.

Children’s diagnostic status in the multicenter trial was evaluated with a diagnostic interview (Diagnostic Interview for Mental Disorders in Children and Adolescents—Kinder-DIPS-OA; Schneider et al., 2017), while in the convenience sample the diagnostic status was based on self-report (parents were asked whether their child has a current or past mental disorder). To check for anxiety symptoms, children and parents filled out a standardized self-report questionnaire (Spence Children’s Anxiety Scale Child and Parent Versions–SCAS-C/P; Spence, 1998). As the study with the convenience sample was originally designed to assess fear conditioning in healthy children and adolescents, the SCAS was the only measurement to check for anxiety symptoms. Nine children exceeded the SCAS cut-off of $T > 60$ (available from [www.scaswebsite.com](http://www.scaswebsite.com)) either in the child or parent version. These children, therefore, had to be classified as having elevated symptoms. As it was unclear whether they had an anxiety diagnosis, they were excluded from further analysis. Hence, the final sample ($N = 274$; age $M = 11.10, SD = 2.14$) included children and adolescents with the following primary diagnoses: 29.2% ($n = 80$) separation anxiety disorder, 23.4% ($n = 64$) social anxiety disorder, 26.6% ($n = 73$) specific phobia, and 20.8% ($n = 57$) non-anxious controls.

All participants and their legal guardians (in most cases parents) provided written informed consent. Both studies were conducted in accordance with the Declaration of Helsinki, the German Federal Data Protection Act, and the GCP-guideline. The Ethics Committee of the Ruhr University Bochum approved both studies.

**Measures**

Diagnostic interview for mental disorders in children and adolescents (Kinder-DIPS-OA). Children and adolescents from the multicenter RCT were diagnosed using the Kinder-DIPS-OA (Schneider et al., 2017) by certified assessors. It consists of two interview versions: one for the child and the other one for the parent or caregiver in which most of the relevant mental disorders in children and adolescents are covered. Severity of diagnoses is rated by clinicians on a scale ranging from 0 to 8, with a rating of ≥ 4 judged as clinically relevant. The Kinder-DIPS-OA has proven to be valid and reliable diagnosing mental disorders in children and adolescents (for an overview of the psychometric properties see: Margraf et al., 2017; Neuschwander et al., 2013). Current diagnoses were based on composite information from both versions of the interview.

Spence children’s anxiety scale child and parent versions (SCAS-C/P). The SCAS is a widely used questionnaire to assess the severity of DSM-IV AD symptoms. It consists of a child (SCAS-C; Spence, 1998) and parent/caregiver (SCAS-P; Nauta et al., 2004) report questionnaire. Each questionnaire measures six domains of anxiety (i.e., generalized anxiety, panic/agoraphobia, social phobia, separation anxiety, obsessive compulsive disorder, and physical injury fears) and consists of 38 items. A total anxiety score can be calculated by summing up the anxiety symptom items. For both studies, the German translation of the SCAS was used,
which has shown excellent psychometric properties in its validation study (Essau et al., 2002). For the present studies, internal consistencies for the SCAS-C and SCAS-P were very good. The value for Cronbach’s Alpha for the SCAS-C was $\alpha = .89$ and for the SCAS-P $\alpha = .89$.

**Fear conditioning paradigm**

For both studies, the paradigm consisted of pre-conditioning, acquisition, and extinction phases. In line with previous fear conditioning paradigms investigating children and adolescents, a sound stimulus was used as a US in both studies (Shechner et al., 2014). The aversive acoustic US was a female scream from the International Affective Digitized Sounds Database (IADS; Bradley & Lang, 2007) with a duration of 3 seconds. It was presented at an intensity of 80 dB binaurally through headphones (DT 770M, Beyerdynamics GmbH, Germany). Psychophysiological data (ECG, startle and SCR) were recorded during the task but as they are not relevant for the present analyses, they are not further described.

The setup of the fear conditioning paradigms in both studies was largely the same (see Adolph et al. (2022) for a detailed description); only the CS stimuli differed. In the multicenter study, two male faces shaded in either blue or yellow served as CS+ and CS-. The paradigm was adapted according to a fear conditioning paradigm developed for adults (Hollandt et al., 2020; Ridderbusch et al., 2021). In the convenience study, two female faces served as CS+ and CS-. In addition, in this study, the acoustic US was accompanied by a picture of a screaming female face who was the same as the one in the CS pictures (in the multicenter study, the US was not accompanied by a picture).

**Procedure**

In the multicenter RCT, the fear conditioning paradigm was conducted at baseline assessments prior to any treatment sessions. After providing informed consent, participants were asked to fill out several questionnaires. Upon arriving at the lab, children and adolescents were given detailed information about the study content and procedure. The experiment was explained in detail, and children were instructed that the scream stimulus might cause discomfort. Only after the child was signaling full understanding of the experimental procedure and gave written assent, the experiment was started. They were then comprehensively instructed on how to give valence and arousal ratings, as well as US expectancy ratings in several example trials. All scales were language-free. For a detailed description on how the scales were explained to the children and adolescents, see Adolph et al. (2022).

Prior to the beginning of the first trial, the US was presented to the children and adolescents and they were asked to rate their arousal (“how aroused did you feel when you were listening to the scream?”) and valence (“how good or bad did you feel when you were listening to the scream?”) on a scale ranging from 0 (not aroused/not good) to 100 (very aroused/very good). For each phase (pre-conditioning, acquisition, and extinction), the instructions were depicted on a computer screen.

**Statistical analyses**

**Frequency of dropouts and dropout reasons.** Dropout was defined as children and adolescents who did not complete the task. Frequency of and reasons for dropouts were explored using a descriptive approach.

**Specific characteristics of participants who discontinued.** To assess whether age, US valence, and arousal rating as well as anxiety symptoms are associated with dropout of the paradigm, point biserial correlations were calculated. For gender and diagnostic status chi-square tests were computed.

**Prediction whether participants discontinue the fear conditioning paradigm.** To assess whether it can be predicted if a child discontinues the fear conditioning paradigm, a logistic regression with dropout (yes/no) as outcome variable was calculated. From the analysis of specific characteristics, the characteristics that were significantly associated with dropout were used as predictors. The strength of the association between dropout and the predictors is represented by the odds ratio (OR). For ease of interpretation, continuous predictors were standardized. Two logistic regressions were calculated: one including the general diagnostic status (presence of an AD vs no presence of an AD) and a second one to check for possible differences between the different ADs using non-anxious controls as reference category.

**Results**

**Frequency of dropouts and dropout reasons**

Of the 274 children and adolescents included in the analyses, 24.1% ($n = 66$) discontinued. Most of them stopped the paradigm after the first presentation of the US or right after the beginning of the acquisition phase. Various reasons for dropout were noted: 59.1% ($n = 39$) were afraid of the scream, 15.2% ($n = 10$) named the startle probe to be too loud or scary, 7.6% ($n = 5$) were afraid of the scream and the startle probe, 6.1% ($n = 4$) dropped out due to technical problems, 6.1% ($n = 4$) did not return for the second day for unknown reasons, 1.5% ($n = 1$) showed an allergic reaction to the electrodes, and for 4.5% ($n = 3$), no specific reason for dropout was named. Nine subjects were excluded from further analysis since dropouts related to technical issues
(n = 1) and allergic reactions (n = 1) were related to the experiment rather than to the children themselves. Similarly, it was not clear whether children and adolescents who did not return for the second day for unknown reasons (n = 4) discontinued because of the experiment or other reasons (e.g., sickness).

**Specific characteristics of participants who discontinued**

To assess which characteristics were associated with dropout of the fear conditioning paradigm, point biserial correlations and chi-square tests were calculated. Age, as well as the arousal rating of the US was significantly associated with dropout of the fear conditioning paradigm (see Table 1 for an overview of the correlations). In addition, the diagnostic status was also significantly associated with dropout, while there was no significant difference between female and male participants with respect to dropout (see Table 2 for an overview of the chi-square tests).

**Prediction whether participants discontinue the fear conditioning paradigm**

As age, arousal rating, and diagnostic status were significantly associated with dropout of the paradigm, they were included as predictors in a logistic regression model (Model I). Age and diagnoses were significant predictors of dropout; arousal rating almost reached significance. Specifically, children and adolescents who were younger and had a primary diagnosis of an AD were more likely to discontinue the fear conditioning paradigm (see Table 3 for the specific results of the logistic regression).

To test whether children and adolescents with a specific AD diagnosis were more likely to drop out, the logistic regression model was repeated with the specific primary AD diagnosis as predictor (see Table 3, Model II). Age remained a significant predictor and again arousal almost achieved significance. All AD diagnoses were tested against non-anxious controls, using indicator contrasts. Participants with an AD were more likely to discontinue (Table 3). Further logistic regression models choosing the specific ADs as reference categories revealed no significant differences between the ADs in predicting dropout of the paradigm (all ps > .05).

In order to evaluate effects found in our sample, post hoc power analyses were conducted using G*Power (Faul et al., 2009). Post hoc power analyses revealed that for standardized variables odds ratios of 0.58 could be found with a power of 0.80 and taking a power of 0.90 odds ratios of 0.53 would be detectable. For inverse effect direction odds ratios of 1.73 could be found with a power of 0.80 and odds ratios of 1.88 with a power of 0.90.

**Discussion**

To the best of our knowledge, the present study is the first to investigate in depth the reasons for dropout from a fear conditioning/extinction paradigm and the characteristics of children and adolescents who discontinue. The main aim was to examine whether a prominent reason for dropout can be identified and if dropout could be predicted by specific characteristics. Almost 25% of the children and adolescents

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**Table 1.** Point-biserial correlations for dropout and age, Spence Children’s Anxiety Scale Parent and Child Version, and valence and arousal rating of the unconditioned stimulus.

|                      | Dropout | Age | SCAS-P | SCAS-C | Valence rating | Arousal rating |
|----------------------|---------|-----|--------|--------|----------------|---------------|
| Dropout              | 1       |     |        |        |                |               |
| Age                  |         | 1   | 0.10   | 0.08   | −0.11          | 0.14*         |
| SCAS-P               |         |     |        |        |                |               |
| SCAS-C               |         |     |        |        |                |               |
| Valence rating       |         |     |        |        | 1              | −0.19***      |
| Arousal rating       |         |     |        |        |                | 0.20***       |

Note. SCAS P/C = Spence Children’s Anxiety Scale Parent and Child Version; US = unconditioned stimulus. *p < .05; **p < .01.

**Table 2.** Chi-square tests for the association between dropout and sex and dropout and primary diagnosis of an anxiety disorder.

|                      | Dropout | Chi-square ($\chi^2$) |
|----------------------|---------|----------------------|
| Gender               | No      | Yes                  |
| Female               | 119     | 32                   |
| Male                 | 89      | 25                   |
| Diagnostic status    |         |                      |
| Non-anxious controls | 52      | 4                    |
| AD diagnosis         | 165     | 53                   |

Note. AD = anxiety disorder.
discontinued the fear conditioning paradigm. Most of the children and adolescents discontinuing reported the aversive scream US and/or the startle probe as the main reasons for dropout. Non-completers were younger and more likely to belong to the sample diagnosed with an AD than completers. US arousal rating was not predictive of dropout from the paradigm. Unexpectedly, sex and US valence rating were not associated with dropout of the fear conditioning paradigm.

Looking at the reasons to discontinue, our results are in line with previous studies (Den et al., 2015; Glenn et al., 2012; Jackson et al., 2017). The scream US was the most prominent reason for dropout of the fear conditioning paradigm followed by fear of the startle probe. Hence, anxiety in response to the experimental stimuli can be identified as the main reason to discontinue the paradigm. Unexpectedly, sex and US valence rating were not associated with dropout of the fear conditioning paradigm.

Looking at the reasons to discontinue, our results are in line with previous studies (Den et al., 2015; Glenn et al., 2012; Jackson et al., 2017). The scream US was the most prominent reason for dropout of the fear conditioning paradigm followed by fear of the startle probe. Hence, anxiety in response to the experimental stimuli can be identified as the main reason to discontinue the fear conditioning paradigm, employing the female scream as US. It is questionable whether this depends on the volume or nature of the scream. However, Shechner et al. (2015) did not find a difference in dropout rates between the female scream paradigm and a paradigm using an aversive sound, indicating that dropout might be related to the volume. This assumption is obvious as children’s sensitivity to loud noises is still subject to development and maturational experience and normalizes when the child grows up (Kennedy et al., 2018). This could make younger children more susceptible to loud noises.

The specific characteristics of the children and adolescents who discontinued the fear conditioning paradigm partly correspond to previous findings. Our findings are in line with Britton et al. (2013) who reported that children who discontinued the fear conditioning paradigm were more anxious and younger than completers. There was no significant association between sex and dropout in our sample, contrary to Glenn et al. (2012) who described non-completers being more likely to be female and Lau et al. (2008) who identified males as being least likely to return for extinction. These mixed findings might be due to differing sample characteristics, as Glenn et al. (2012) only reported results of a healthy control sample and Lau et al. (2008) reported results of children with a generalized anxiety disorder, social anxiety disorder, separation anxiety disorder, and healthy controls. In addition, the patient sample size was rather small. Samples covering the entire AD spectrum as well as healthy controls are needed to clarify the relationship of participant gender and dropout. To prevent dropout in future studies, several aspects can be considered: analogous to the shock workup that is done with adults prior to fear conditioning, the volume of the scream could be adjusted according to children’s fear ratings. Before starting the actual experiment, children and adolescents could be asked to rate their fearfulness of the scream, and a volume that is tolerable, but still fearful, could be chosen for the subsequent experiment. Recently, Beaurenaut et al. (2020) could show that low intensity screams still elicit anxiety while being more tolerable and less harmful.

Taking a closer look at the scream as US, it could be that it is less tolerable than other US established in fear conditioning paradigms, for example, scratching noises (Neumann et al., 2008) or an aversive alarm (Shechner et al., 2015). Future studies are needed to compare different types of US, not just regarding conditionability, but especially looking at dropout rates and acceptance by participants. In addition, it would be interesting to test whether paradigms and especially US used with adults would be suitable and ethically acceptable for children and adolescents.

Furthermore, subsequent analyses should evaluate whether dropout of the fear conditioning paradigm is a

Table 3. Logistic regression models.

| Model | OR   | 95% CI      |
|-------|------|-------------|
| Model I |      |             |
| Age   | 0.40*** | [0.25, 0.65] |
| Arousal rating | 1.42a | [0.98, 2.04] |
| Diagnostic status (yes/no) | 7.24** | [2.03, 25.78] |
| Model II |      |             |
| Age   | 0.40*** | [0.24, 0.65] |
| Arousal rating | 1.43b | [0.99, 2.07] |
| Primary diagnosis |      |             |
| Separation AD versus non-anxious controls | 6.82** | [1.80, 25.84] |
| Social AD versus non-anxious controls | 7.79** | [1.74, 34.84] |
| Specific phobia versus non-anxious controls | 7.68** | [1.92, 30.71] |

Note. AD = anxiety disorder; OR = odds ratio; CI = confidence interval.
a p = .062.
b p = .059.
c p < .01; d p < .001
potential treatment predictor of exposure-based CBT. Children and adolescents who discontinue a fear conditioning paradigm could be more prone to avoid fearful situations and therefore might also be more likely to avoid exposure sessions during therapy. Thus, analogous to, for example, pre-treatment cardiac vagal tone (Wendt et al., 2018) or fear extinction learning (Geller et al., 2019), dropout of the fear conditioning paradigm could be a potential predictor of treatment outcome.

Dropout rates and specific reasons for dropout need to be considered when interpreting results of fear conditioning paradigms with children and adolescents as they could harm generalizability of the results. High dropout rates could lead to a systematic underrepresentation of a specific group and to conclusions that are not transferable to the whole sample. Based on inappropriate assumptions, findings might be generalized to populations that were underrepresented in the study sample. Future studies should identify a US that eliminates dropout in order to study conditioning and extinction effects in all children and adolescents.

Limitations

Children and adolescents in the convenience sample were not diagnosed with a structured clinical interview. However, all parents and children stated by self-report not to have a current childhood AD. This was further supported by a well validated questionnaire with normed cut offs. Even if the diagnostic status was not assessed identical, the current trial is still valuable as it is a first attempt to research non-completers. Future studies should also assess the healthy control sample with a structured interview in order to include the clinical severity rating as a possible predictor of dropout.

Additionally, as this analysis was assembled post hoc based on variables already included in the previous trials, it was only possible to make use of questionnaires that had been used in these trials. Further studies should assess a broader set of cognitive and/or temperamental variables that might be associated with dropout.

The procedure of the fear conditioning paradigms used in both studies were slightly different. Though this does not influence the rate and/or reasons for dropout as all children dropped out either prior to acquisition or during the first acquisition trials. Both paradigms were identical till then.

Last but not least, analyses have to be considered in light of the selection of participants when studying anxious individuals in the laboratory. Due to the nature of laboratory studies and the participants’ anxiety, research may already be limited to a subsample of participants agreeing to participate and thus specific characteristics may be underrepresented in the study population. However, in the present two studies agreement to participate in the experimental session was high. All control children from the non-clinical convenience sample gave their informed consent to participate in the experimental session. Acceptance was also high within the multicenter RCT, as more than two thirds of children with an AD agreed to participate in the fear conditioning paradigm. In addition, those who gave informed consent did not differ from those who did not give informed consent in terms of age ($\chi^2 (1) = -1.35, p = .18$), gender ($\chi^2 (1) = 0.02, p = .90$), and type of anxiety diagnosis ($\chi^2 (2) = 0.77, p = .68$). Thus, the current sample can be considered representative for the total patient sample.

Conclusion

From an ethical and scientific perspective, future studies should pay close attention to dropout rates and reasons as well as investigate whether specific characteristics of children and adolescents who discontinue can be identified. Dropouts may affect external validity and thus, studies should carefully analyze whether the results may be affected by dropouts and whether the sample of non-completers differs from the completer sample. These are important factors to consider when interpreting the results of fear conditioning and extinction paradigms, as these are the central mechanisms underlying exposure-based CBT.

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