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SimSAARlabim study – The role magic tricks play in reducing pain and stress in children

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ABSTRACT

Background: Vaccination is an essential preventative medical intervention, but needle fear and injection pain may result in vaccination hesistancy.
Study purpose: To assess the role of magic tricks – no trick vs. one trick („disappearing handkerchief trick“) vs. three tricks (“disappearing handkerchief trick“, “jumping rubber band trick“, and “disappearing ring trick“) – performed by a professional magician and pediatrician during routine vaccination in reducing discomfort/pain and the stress response (heart rate, visual analogue scale (VAS), and biomarkers (cortisol, Immunoglobulin A (IgA), α-amylase, and overall protein concentration in saliva before and after vaccination).
Patients and methods: Randomized controlled trial (RCT) in healthy children aged 6–11 years undergoing routine vaccination in an outpatient setting.
Results: 50 children (26 female) were enrolled (no trick: n = 17, 1 trick: n = 16, 3 tricks: n = 17) with a median age of 6.9 years (range: 5.3–10.8 years). We detected no significant differences among the three groups in their stress reponse (heart rate before and after vaccination and cortisol, IgA, α-amylase, and overall protein concentrations in saliva before and after vaccination) or regarding pain assessment using the VAS.
Conclusions: Although children undergoing routine outpatient vaccination appeared to enjoy a magician's presence, the concomitant performance of magic tricks revealed no significant effect on the stress response.

1. Introduction

Vaccination is the most frequent painful procedure that healthy children and adolescents undergo. Unmitigated pain and fear cause unnecessary suffering and negative vaccination experiences for children and their parents/caregivers in the short-term, while in the long-term such negative experiences can develop into needle phobia, which in turn can trigger vaccine hesitancy and outbreaks of preventable diseases [1]. The Strategic Advisory Group of Experts on Immunization (SAGE) concluded that vaccine hesitancy constitutes a delay in acceptance or refusal of vaccination despite availability of vaccination services [2]. Needle fear and negative attitudes can persist, contributing considerably to non-compliance in adulthood. Moreover, as adults can also transfer their fears to their children, this has a negative impact on the next generation.

Reducing fear/phobia of needles is therefore essential to promote large-scale vaccination programs successfully. In children, blood injection injury phobia episodes of up to 20 % have been reported recently, with age-dependent prevalence rates of 3–8 % [3], Although there is a plethora of evidence-based pharmacological and non-pharmacological interventions available to mitigate fear and pain during painful procedures such as vaccination [4], utilization of these interventions in clinical routine is sub-par, and few professionals have actually integrated these methods in everyday clinical practice. Non-pharmacological analgesia refers to the use of prophylactic and complementary interventions aimed at alleviating pain without applying medication. The mechanisms of action of these interventions are heterogeneous. While some induce the release of endogenous endorphins,

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others activate certain neuropeptide systems with the ultimate effect of enhancing the action of endogenous opiates, while still others aim to distract from pain.

The most frequently applied non-pharmacological methods nowadays to alleviate pain during vaccination have been breastfeeding and distraction measures [5]. Distraction is a method in which a caregiver (parent, nurse, physician, magician) attends an examination or procedure that the child finds "threatening" to support the child's natural coping skills, or to help the child relax by focusing attention on something other than the medical procedure.

To the best of our knowledge, no published report has evaluated the role of magic tricks performed by a professional magician in reducing the "stress response" associated with painful procedures, including routine vaccinations in children.

The aim of this randomized controlled trial was therefore to assess whether the concomitant perfomance of magic tricks would reduce the "stress response" in children aged 6–11 years undergoing routine vaccination procedures in an outpatient setting.

2. Patients and methods

2.1. Study design

Healthy study participants (6–11 years of age) with no chronic

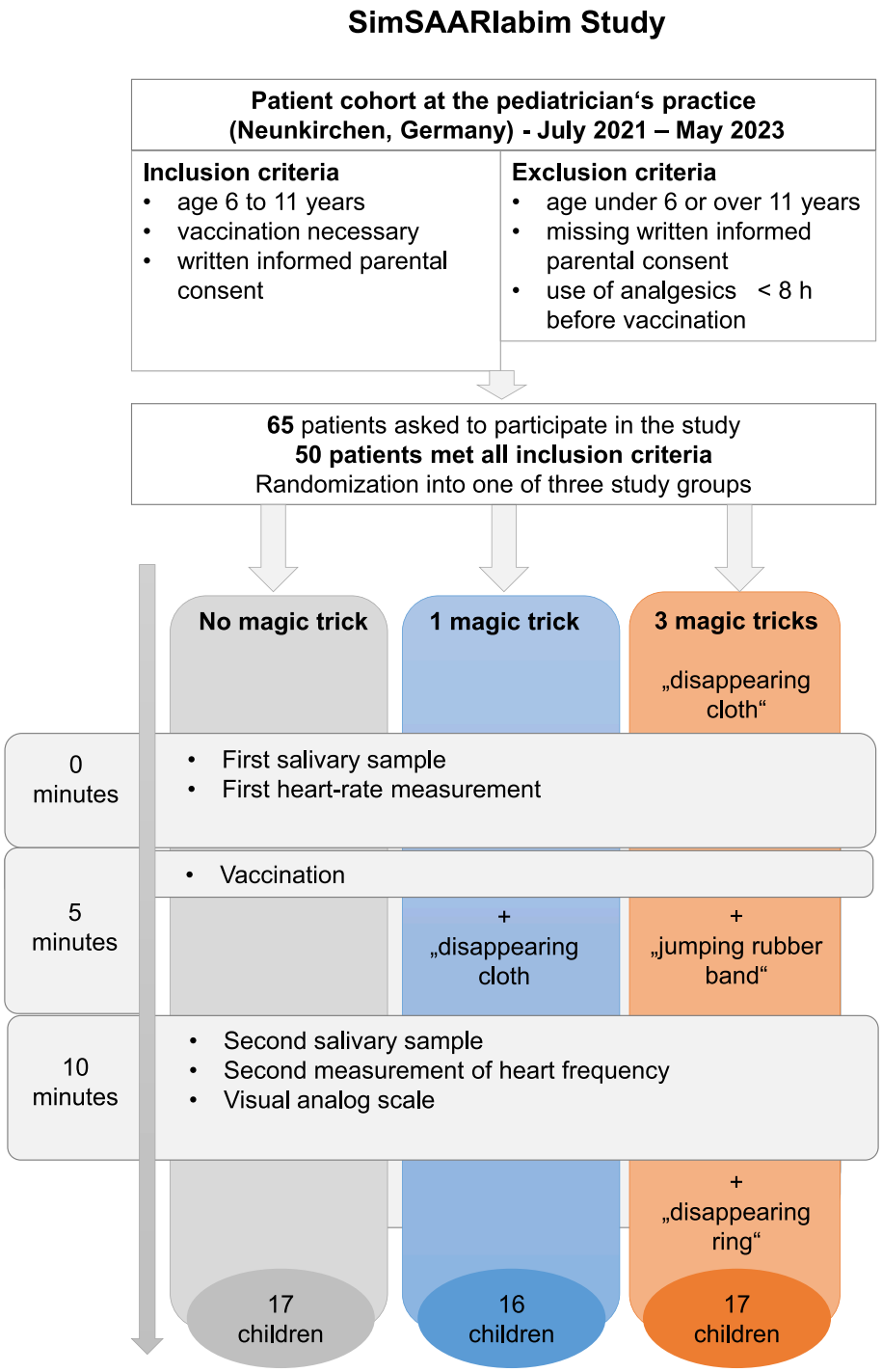

Fig. 1. Trial design.

medical condition were vaccinated according to the STIKO (Ständige Impfkommission, Robert Koch-Institut, Berlin, Germany) recommendations or received an influenza vaccination at their pediatrician's office. The study participants were divided into three groups: group 1 watched one magic trick ("The disappearing cloth/handkerchief trick" during vaccination (https://www.youtube.com/watch?v=cgaX6qQ3Chc), group 2 watched three magic tricks ("the disappaering cloth/handkerchief trick", "the jumping rubber band trick" (https://www.youtube.com/watch?v=TF-05tb_gck), and "the disappearing ring trick" (https://www.youtube.com/watch?v=WAaEQV-Rxp0) before, during and after vaccination), and group 3 served as a control group since they saw no magic trick demonstration (Fig. 1). All magic tricks were performed in-person by A. N. While the first trick was played, baseline assessment was performed, the second trick was played during vaccination, and the third trick was playedafter the vaccination procedure. All children were selected from one out-patient clinic, and enrolled consecutively after parental consent was obtained.

The SimSAARlabim study was designed and performed in accordance with the Declaration of Helsinki, and approved by the regional ethics committee of Saarland, Saarbrücken, Germany (file number 72/21). Written informed consent was obtained from parents or guardians prior to the vaccination. Trial subjects were excluded in case of age <6 years and >11 years, missing written informed consent and/or consumption of analgesics <8 h before vaccination. All collected data were pseudonymized. The SimSAARLabim study is registered with the German Clinical Trials Register (DRKS-ID: DRKS00025832).

2.2. Heart rate measurements

Heart rate was measured both 5 min before and after vaccination.

2.3. Assessment of pain intensity

Subjective pain intensity was assessed using the standardized Visual Analogue Scale (VAS). To avoid distortions in pain perception, this study included only those children not taking analgesics for at least 8 h before the vaccination procedure.

2.4. Saliva sampling & laboratory assays

Saliva was collected using the absorbent roll Salivette® cortisol (51.1534.500, Sarstedt, Numbrecht, Germany) according to manufacturer's instructions. Salivary samples were taken both 5 min before and after vaccination. Participants placed a Salivette in their mouths for 2 min with light jaw movements to stimulate the saliva flow. To avoid saliva contamination, participants were asked to refrain from consuming solid and liquid foods, chewing gum, and brushing their teeth at least 60 min before sampling. Salivettes were stored up to five days at 4 °C in the pediatrician's office followed by centrifugation at 1000*g* for 2 min at room temperature at the Departement of General Pediatrics and Neonatology, Homburg, Germany. Salivary samples were stored at −20 °C until analysis. A minimum of 200 µL of saliva was required to process the sample.

Stress-associated protein levels were quantified using enzyme immunoassays of IBL International GmbH, Hamburg, Germany. Cryopreserved salivary samples were frozen/thawed and prepared for quantitative analysis of free cortisol (RE52611), α-amylase activity (RE80111) and IgA (DM59171).

Total protein concentration of saliva samples was quantified using Pierce™ BCA Protein Assay Kit (ThermoScientific™, Waltham, MA, USA).

Analyses were all performed according to manufacturer's instructions for use. Absorbance was measured using microplate reader Infinite M Plex® (Tecan Trading AG; Männedorf, Switzerland).

2.5. Statistical analysis

Our primary outcome parameter was a drop in the VAS by one (e.g., from 7 (control group) to 6 (two intervention groups with one and three magic tricks)). Group sample sizes of 21 are needed to achieve 81.50 % power to reject the null hypothesis of equal means when the population mean difference is µ1 - µ2 = 7.0–6.0 = 1.0 with a standard deviation for both groups of 1.0 and with a significance level (alpha) of 0.025 using a two-sided two-sample equal-variance *t*-test. Given a drop-out rate of 20–25 %, a sample size of 27 (each group) was required.

Statistical analysis was performed using IBM SPSS Statistics (IBM Corp. Released 2021. IBM SPSS Statistics for Macintosh, Version 29.0.0.0. Armonk, NY: IBM Corp). Quantitative data was examined for normal distribution using Shapiro-Wilk test. In the first step, we assessed overall differences among the three study groups applying various statistical tests: the Kruskal-Wallis test for non-metric or non-normally distributed variables (e.g., concentration of specific or total protein levels), analysis of variance for metric, normally distributed variables (e.g., heart rate before/after the interventions), and the Chi-Square test/Fisher's exact test for nominal variables. In the second step, we employed univariate linear regression analysis to examine the effect of predefined contrasts among the three study groups [contrast one: no magic trick vs. (one magic trick & three magic tricks); contrast two: one magic trick vs. three magic tricks] on pain assessment using the VAS and stress response parameters (heart rate after vaccination, cortisol, IgA, α-amylase, and overall protein concentrations after vaccination) while considering additionally the initial stress response parameters.

Our study data was analyzed on an intention-to-treat basis.

3. Results

Due to subpar study participation, we were able to only assess a total of 65 children for eligibility between 07/2021 and 05/2023. 15 patients were subsequently excluded (11 patients failed to show up for their appointment, 3 lacked parental consent, 1 other reason). We ultimately enrolled 50 children (26 female, 24 male) in the SimSAARlabim trial (Fig. 1) aged a median 6.9 years (range: 5.3–10.8 years). Patients were randomized to the study groups as follows: no trick: n = 17, 1 trick: n = 16 and 3 tricks: n = 17.

No statistically significant differences appeared among the three groups in relevant patient demographics including vaccination type, as

Table 1
Patient's characteristics. Data are illustrated as absolute numbers and percentage respectively median and range.

	Overall n = 50	No magic trick n = 17	One magic trick n = 16	Three magic tricks n = 17	p-value
Gender					0.68#
male	24 (48.0 %)	7 (41.2 %)	9 (56.3 %)	8 (47.1 %)	
female	26 (52.0 %)	10 (58.8 %)	7 (43.8 %)	9 (52.9 %)	
Age [years]	6.9 (5.3–10.8)	7.0 (5.3–10.8)	6.5 (5.4–10.5)	7.5 (5.5–10.3)	0.23+
Vaccine	48	15	16	17	0.84*
Gardasil	4 (8.3 %)	1 (6.7 %)	2 (12.5 %)	1 (5.9 %)	
Boostrix	19 (39.6 %)	5 (33.3 %)	5 (31.3 %)	9 (52.9 %)	
FSME	14 (29.2 %)	6 (40.0 %)	5 (31.3 %)	3 (17.6 %)	
Havrix	1 (2.1 %)	0 (0.0 %)	1 (6.3 %)	0 (0.0 %)	
Influsplit tetra	9 (18.8 %)	3 (20.0 %)	3 18.8 %)	3 (17.6 %)	
Boostrix & FSME	1 (2.1 %)	0 (0.0 %)	0 (0.0 %)	1 (5.9 %)	

Fisher's exact test (*) if one of the expected cell frequencies was <5, Chi2 test if all the expected cell frequencies were ≥5 (#).
Kruskal-Wallis test (+) for non-metric or metric, non-normally distributed variables.

illustrated in Table 1. Moreover, the three groups did not differ significantly in their pain assessments using the VAS (Table 1) or in their stress reponses (heart rate before and after vaccination and cortisol, IgA, α-amylase and overall protein concentrations in saliva before and after vaccination) (Table 2). Nor did their saliva samples reveal any significant difference (Table 2). Also, no significant differences existed between heart rate before versus after vaccination and cortisol, IgA, α-amylase and overall protein concentrations in saliva before versus after vaccination within the study groups - exept for increases in IgA and α-amylase levels before versus after vaccination in the group with 3 tricks (each $p = 0.03$).

As detailed in table 3 and 4, univariate linear regression analysis failed to demonstrate any significant influence among our three study groups' specific conditions, namely no trick vs. 1 or 3 tricks, as well as 1 trick vs. 3 tricks – on pain assessment using the VAS and stress response parameters (heart rate after vaccination as well as cortisol, IgA, α-amylase and overall protein concentrations after vaccination).

Stress response parameters before vaccination revealed a significant impact on stress response parameters after vaccination (Tables 3 and 4): heart rate ($b = 0.48$), cortisol ($b = 0.93$), IgA ($b = 1.12$), α-amylase ($b = 0.87$), and overall protein ($b = 0.78$). Moreover, the overall protein concentration before vaccination proved to be an independent influential variable on IgA and α-amylase concentration after vaccination ($b = 0.05$ and $b = 0.11$) (Table 4). Conversely, IgA and α-amylase concentrations before vaccination were evidently significant independent influential variables on the overall protein concentration after vaccination ($b = 7.67$ and $b = 2.9$) (Table 4).

4. Discussion

In this prospective RCT, we failed to demonstrate that the performance of magic tricks (one or three vs. no magic trick) had a clinically significant effect on the stress response associated with routine vaccinations in children aged 6–11 years, except for statistically significant increases in IgA and α-amylase levels before versus after vaccination in the group with 3 tricks (each $p = 0.03$). This may be attributable to an already low stress level prior to the vaccination procedure itself, in part secondary to the overall relaxed atmosphere in this particular outpatient clinic, as the physician/magician (A. N.) was very well known to all participating children.

Our comprehensive assessment of the stress response in our study cohort involed a self-assessment tool (VAS), a readily available physiological parameter (heart rate) and biochemical parameters (cortisol, IgA, α-amylase, and overall protein concentrations in saliva).

Table 2
Saliva characteristics. Data are illustrated as absolute numbers and percentage respectively median and range.

	Overall n = 50	No magic trick n = 17	One magic trick n = 16	Three magic tricks n = 17	p-value
Heart rate before vaccination [bpm]	88.0 (60.0–126.0)	88.0 (76.0–100.0)	90.0 (60.0–112.0)	88.0 (64.0–126.0)	0.76°
Heart rate after vaccination [bpm]	92.0 (64.0–126.0)	96.0 (80.0–116.0)	92.0 (64.0–126.0)	88.0 (64.0–116.0)	0.88°
Visual analogue scale (after vaccination)					0.61+
0					
1	24 (50.0 %)	7 (43.8 %)	9 (60.0 %)	8 (47.1 %)	
2	1 (2.1 %)	1 (6.3 %)	0 (0.0 %)	0 (0.0 %)	
3	9 (18.8 %)	3 (18.8 %)	3 (20.0 %)	3 (17.6 %)	
4	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	
5	9 (18.8 %)	3 (18.8 %)	2 (13.3 %)	4 (23.5 %)	
6	1 (2.1 %)	1 (6.3 %)	0 (0.0 %)	0 (0.0 %)	
7	2 (4.2 %)	1 (6.3 %)	1 (6.7 %)	0 (0.0 %)	
8	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	
9	1 (2.1 %)	0 (0.0 %)	0 (0.0 %)	1 (5.9 %)	
10	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	
	1(2.1 %)	0 (0.0 %)	0 (0.0 %)	1 (5.9 %)	
Saliva sample available					1.0*
Yes	47 (94.0 %)	16 (94.1 %)	15 (93.8 %)	16 (84.1 %)	
No	3 (6.0 %)	1 (5.9 %)	1 (6.3 %)	1 (5.9 %)	
Timespan between waking up and first sampling [h]	3.8 (0.8–10.5)	4.1 (1.5–9.0)	4.3 (1.5–9.8)	3.4 (0.8–10.5)	0.72+
Eating 60 min before sampling					0.30*
Yes	4 (8.5 %)	1 (6.3 %)	0 (0.0 %)	3 (18.8 %)	
No	43 (91.5 %)	15 (93.8 %)	15 (100.0 %)	13 (81.3 %)	
Drinking 60 min before sampling					0.23*
Yes	8 (17.0 %)	2 (12.5 %)	1 (6.7 %)	5 (31.3 %)	
No	39 (83.0 %)	14 (87.5 %)	14 (93.3 %)	11 (68.8 %)	
Chewing gum 60 min before sampling					0.32*
Yes	1 (2.1 %)	0 (0.0 %)	1 (6.7 %)	0 (0.0 %)	
No	46 (97.9 %)	16 100.0 %)	14 (93.3 %)	16 (100.0 %)	
Tooth brushing 60 min before sampling					1.0*
Yes	3 (6.4 %)	1 (6.3 %)	1 (6.7 %)	1 (6.3 %)	
No	44 (93.6 %)	15 (93.8 %)	14 (93.3 %)	15 (93.8 %)	
Timespan between samples [min]	10.0 (3.0–22.0)	10.0 (3.0–15.0)	10.0 (5.0–15.0)	10.0 (9.0–22.0)	0.33+
Saliva volume before vaccination [µl]	800.0 (50.0–1800.0)	675.0 (140.0–1550.0)	900.0 (50.0–1800.0)	835.0 (100.0–1500.0)	0.41+
Saliva volume after vaccination [µl]	650.0 (50.0–1800.0)	465.0 (120.0–1400.0)	850.0 (50.0–1650.0)	625.0 (50.0–1800.0)	0.67+
Cortisol before vaccination [µg/dl]	0.06 (0.004–0.46)	0.06 (0.02–0.46)	0.05 (0.004–0.42)	0.10 (0.01–0.16)	0.31+
Cortisol after vaccination [µg/dl]	0.07 (0.01–0.46)	0.07 (0.02–0.41)	0.06 (0.01–0.46)	0.08 (0.03–0.21)	0.35+
IgA before vaccination [µg/ml]	26.1 (1.0–129.4)	35.1 (1.4–49.4)	26.1 (1.0–68.5)	19.6 (5.9–129.4)	0.65+
IgA after vaccination [µg/ml]	30.5 (2.5–170.1)	32.3 (2.5–69.1)	28.3 (2.9–82.7)	34.3 (5.2–170.1)	0.86+
α-amylase before vaccination [U/ml]	78.1 (17.8–296.0)	95.4 (44.1–296.0)	78.1 (20.3–184.4)	67.3 (17.8–205.8)	0.44+
α-amylase after vaccination [U/ml]	95.8 (20.8–277.7)	78.7 (35.0–277.7)	95.8 (35.5–185.8)	103.6 (20.8–235.3)	0.92+
Overall protein concentration before vaccination [µg/ml]	969.2 (515.6–1916.6)	1032.7 (757.7–1413.7)	993.8 (569.7–1300.5)	888.9 (515.6–1916.6)	0.52+
Overall protein concentration after vaccination [µg/ml]	1069.0 (556.7–1471.1)	1181.4 (707.0–1453.1)	1125.2 (569.4–1399.7)	925.8 (556.7–1471.1)	0.69+

Fisher's exact test (*) if one of the expected cell frequencies was < 5, Chi2 test if all the expected cell frequencies were ≥ 5 (#).
Analysis of variance (°) for metric, normally distributed variables.
Kruskal-Wallis test (+) for non-metric or metric, non-normally distributed variables.

Table 3
Results of univariate linear regression analysis – independent influential variables for nociception (VAS) and heart Rate after vaccination.

	Dependent Variable			
	Nociception (VAS)		Heart rate after vaccination	
Risk factor	Regression coefficient B (95 % CI)	p-value	Regression coefficient B (95 % CI)	p-value
Study group				
1 vs. (2 & 3)	−0.02(1.15, 2.56)	0.98	−1.18(−7.18, 4.82)	0.69
2 vs. 3	0.51 (−0.36, 1.38)	0.24	−0.71(−5.94, 4.52)	0.79
Age at examination	$-0.17 * 10^{-3}$ $(-1.39, 1.05) * 10^{-3}$	0.78	$-4.10 * 10^{-3}$ $(-11.27, 3.07) * 10^{-3}$	0.26
Sex	0.09(−1.32, 1.52)	0.89	9.40 (1.48, 17.32)	0.02
Heart rate before vaccination	0.03 (−0.02, 0.08)	0.26	0.48 (0.192, 0,769)	<0.01
Cortisol before vaccination	1.70(−6.48, 9.88)	0.68	8.94(−38.48, 56.36)	0.70
IgA before vaccination	−0.02(−0.05, 0.01)	0.20	0.002(−0.176, 0.180)	0.98
α-amylase before vaccination	−0.001(−0.013, 0.011)	0.87	0.03(−0.04, 0.10)	0.39
Overall protein concentration before vaccination	$1.95 * 10^{-5}$ (−0.003, 0.003)	0.99	0.014(−0.004, 0.031)	0.12

Stress can betriggered by internal and external influences on an individual by faulty homeostatic equilibrium. Environmental, social, and psychological stress, which exert many negative effects on the organism, can be monitored by measuring various biomarkers [6–9]. Widely accepted physiological biomarkers of stress include the respiratory rate, core body temperature, blood pressure and pulse [6–9], but the stress level can also be determined using biochemical biomarkers in blood and saliva. Saliva is a suitable biospecimen source for investigating stress, as there is solid evidence of a strong correlation between stress levels and the levels of numerous salivary proteins [7,10,11]. Non-invasive salivary biomarkers such as cortisol, salivary a-amylase, and immunoglobulins, among others, appear well-suited for children as collecting saliva is painless, and there is a strong correlation between physical stress levels and the levels of many salivary proteins [7,10,11]. However, hormonal levels can vary among children at different developmental stages and in various health conditions [10]. The hormone cortisol, which is secreted into the blood in response to various stress situations, as well as HPA-axis activation are two of the most important stress markers. The levels of cortisol in blood and in saliva correlate quite closely. Similarly, alpha-amylase in saliva is considered a biomarker of sympathetic stimuli [7]. The release of stress hormones causes impaired immunoglobulin secretion, resulting in a lower immunoglobulin concentration (eg, of IgA) in body fluids [7].

There are pharmacological and non-pharmacological interventions to reduce the stress response and pain associated with routine vaccination and painful procedures in children [6].

Non-pharmacological interventions have been the focus of various studies [4,5,12,13] which investigated the suitability of such interventions to reduce children's anxiety about dental procedures, including the performance of magic tricks, which led to better cooperation in pediatric patients [14].

Magic is grounded in the fundamental principles of perception, deceit, and psychology [5]. By understanding how the human brain processes information, magicians find creative ways to manipulate our perception. Because healthcare revolves around on the functioning of the mind and body, there are several ways by which magic can be applied clinically. While magic is a widely used form of amusement or pastime, the goal of this study was to investigate whether the performance of magic tricks effectively ameliorates the stress response associated with routine vaccination in children aged 6–11 years.

Most children are naturally afraid of needles and report that needle fear and injection pain are the worst part of vaccinations [15]. Pain from injection or fearing needles are relevant barriers to vaccination in children deserving more attention. Despite the plethora of evidence-based interventions available to mitigate fear and pain during vaccination, these interventions are poorly utilized in clinical practice [15].

Some important shortcomings undoubtedly apply to our RCT. Because of subpar recruitment during the Covid-19 pandemic and restrictions – as other studies have described [16] – we were unable to enroll all 81 study participants, and study recruitment was stopped once we had enrolled 50 children.. In doing so, possibly, although very unlikely, a statistically positive effect of magic tricks on the stress response may have been missed. Although we did not manage to recruit as many patients as calculated in our statistical analysis plan, given our

Table 4
Results of univariate linear regression analysis – independent influential variables for cortisol, IgA, α-amylase, and overall protein concentration after vaccination.

	Dependent Variable							
	Cortisol concentration after vaccination		IgA concentration after vaccination		α-amylase concentration after vaccination		Overall protein concentration after vaccination	
Risk factor	Regression coefficient B (95 % CI)	p-value	Regression coefficient B (95 % CI)	p-value	Regression coefficient B (95 % CI)	p-value	Regression coefficient B (95 % CI)	p-value
Study group								
1 vs. (2 & 3)	−0.01(−0.06, 0.03)	0.51	4.08(−8.72, 16.88)	0.52	−10.89 (−37.47, 15.69)	0.41	−44.27 (−190.61, 102.08)	0.54
2 vs. 3	0.01 (−0.03, 0.04)	0.76	4.77(−6.19, 15.73)	0.38	-0.019 (−22.44, 22.06)	0.99	−37.10 (−156.15, 81.96)	0.53
Age at examination	$0.01 * 10^{-3}$ $(0.05, 0.06) * 10^{-3}$	0.78	$18.94 * 10^{-3}$ $(4.40, 33.47) * 10^{-3}$	0.01	$-2.20 * 10^{-3}$ (−34.07, 29.67) $* 10^{-3}$	0.89	0.09(−0.10, 0.28)	0.33
Se	−0.01(−0.07, 0.05)	0.77	6.18 (−11.73, 24.09)	0.49	17.17 (−19.26, 53.50)	0.35	−47.36 (−247.15, 152.43)	0.63
Heart rate before vaccination	0.001 (−0,001. 0.004)	0.26	−0.01 (−0.71, 0.68)	0.97	0.14 (−1.30, 1.58)	0.84	0.26 (−8.12, 8.63)	0.95
Cortisol concentraton before vaccination	0.93(0.84, 1.02)	<0.001	32.14(−65.30, 129.57)	0.51	−45.64 (−227.00, 135.72)	0.61	631.15 (−453.79, 1716.09)	0.24
IgA concentration before vaccination	0.001(0.000, 0.002)	0.14	1.12(0.98, 1.27)	<0.001	0.30 (−0.51, 1.10)	0.46	7.67 (3.13, 12.21)	<0.01
α-amylase concentration before vaccination	$-0.12* 10^{-3}$ (−0.73, 0.50) $* 10^{-3}$	0.87	0.07(−0.01, 0.22)	0.37	0.87 (0.74, 1.03)	<0.001	2.90 (1.36, 4.44)	<0.001
Overall protein concentration before vaccination	$7.21* 10^{-5}$ (−4.67, 19.01) $* 10^{-5}$	0.23	0.05(0.02, 0.07)	<0.001	0.11 (0.04, 0.18)	<0.01	0.78 (0.54, 1.02)	<0.001

"preliminary" study results, it is unlikely that continuing the study would have yielded any statistically significant and clinically meaningful differences among these three groups.

Second, while we observed no major effect in the stress response itself, we cannot exclude with certainty a positive effect of magic tricks on the overall rate of acceptance of vaccinations in children. The use of other biomarkers (eg, catecholamines [17,18]) may have been better suited to detect acute changes in the stress response, but sampling (intravenous, urine) would have been unfeasible in this cohort of young children.

5. Conclusion

Different non-pharmacological interventions can be applied in pediatrics to manage pain associated with acutely painful interventions, but there are significant gaps in the existing literature on the non-pharmacological management of acute pain in infancy [19]. To the best of our knowledge, no RCT before ours assessed the role of magic tricks in alleviating the stress response in children undergoing routine vacctions. Although the children we investigated undergoing routine outpatient vaccination appeared to have enjoyed the presence of a magician, the concomitant performance of magic tricks had no major clinical significant effect on their stress response.

Combining magic tricks with a painful procedure (eg, vaccinations) may prove efficacious in motivating families (parents and children) to undergo routine vaccination procedures and reduce vaccination hesistancy. This is extremely important given the role of childhood vaccinations as a key preventative measure in modern medicine.

6. Authoŕs contributions

Jutta Teichfischer was responsible for study conception, patient treatment, data compilation, and critical revision of the manuscript.

Regine Weber was responsible for selecting laboratory parameters, all laboratory work and analysis, and critically revising the manuscript.

Elisabeth Kaiser was responsible for selecting laboratory parameters, all laboratory work and analysis, and critically revising the manuscript.

Martin Poryo was responsible for data compilation, statistical analysis, and critical review of the manucript.

Julius Johannes Weise was responsible for statistical analysis.

Alexander Nisius was chief magician and creativity director, and was responsible for patient comfort and care beyond belief. He created many unforgettable moments for all children enrolled, and was responsible for critical review of the manuscript.

Sascha Meyer was chief investigator, was responsible for study conception, data analysis, and writing the manuscript.

CRediT authorship contribution statement

Jutta Teichfischer: Formal analysis, Investigation, Project administration, Writing – original draft, Writing – review & editing. **Regine Weber:** Formal analysis, Investigation, Project administration, Writing – original draft, Writing – review & editing. **Elisabeth Kaiser:** Conceptualization, Formal analysis, Investigation, Project administration, Writing – original draft, Writing – review & editing. **Martin Poryo:** . **Julius Johannes Weise:** Data curation, Investigation, Validation, Writing – original draft, Writing – review & editing. **Alexander Nisius:** Conceptualization, Formal analysis, Investigation, Project administration, Resources, Writing – original draft, Writing – review & editing. **Sascha Meyer:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Supervision, Validation, Writing – original draft, Writing – review & editing.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: The authors have no obvious conflict of interests to report, but will – no matter under whatever circumstances – continue to strive for more magic moments for their pediatric patients when undergoing medical treatment.

Data availability

Data will be made available on request.

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Ethics approval was provided by the ethics committee of Saarland, Saarbrücken, Germany (file number: 72/21).

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