Indoor factors and behavioural problems in children: The GINIplus and LISAplus birth cohort studies

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ARTICLE INFO

ABSTRACT

Indoor microbial agents exposure is associated to depressive symptoms in adults and persistent exposure to indoor mould is associated to poorer cognitive function in children. In our study, we aimed to assess the effects of the exposure to indoor factors associated with increased microbial exposure (mould, dampness and pets) on behavioural problems in children aged 10 years, participating in two German birth cohorts. A total of 4860 children were followed until the age of 10 years, and the strengths and difficulties questionnaire (SDQ) was administered to the parents. Indoor factors were assessed through parental reported questionnaires in periodical surveys. Logistic and multinomial regressions adjusting for potential confounders were performed. Prevalences of borderline/abnormal total scores in the SDQ at 10 years of age were higher in children exposed to mould (aOR = 1.23, 95%CI = 1.00–1.56), dampness (aOR = 1.51, 95%CI = 1.10–2.07), and pets (aOR = 1.48, 95%CI = 1.20–1.94). The dimension "emotional symptoms" showed statistically significant risk estimates for mould and pets, meanwhile "conduct problems" and "hyperactivity/inattention" dimensions only did for pets. No significant associations were found for the "peer relationship problems" dimension. We found a significant strong interaction between dampness and pet, the risk of borderline/abnormal scores in the "total difficulties" scale and the "emotional symptoms" dimension for pets' was at least twice the risk in children with reported dampness than in children without. Our findings point to a potential effect of microbial exposure on children's behavioural problems, especially on emotional disorders, probably mediated through neurotoxicity and immune system activation.

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Introduction

Mental health disorders in pre-adolescent and adolescent ages are highly prevalent across countries, ranging from 10% to 20% (Costello et al., 2005; Patel et al., 2007; Belfer, 2008; Ravens-Sieberer et al., 2008). The development of these disorders during childhood is of major public health concern, not only because it contributes to the total burden of diseases during adulthood, but also because it limits the well functioning of the child.

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Several aspects related to home environment have been identified as risk factors for poor mental health in children. Most of these are psychosocial factors related to family structure and functioning (Jenkins and Smith, 1991), illnesses (Barkmann et al., 2007), time spent in front of the television or computer (Guxens et al., 2009), parental unemployment, and socio-economical status (Wille et al., 2008). Nevertheless, other indoor factors have shown to increase the risk of behavioural or neurodevelopment problems in children. For example, environmental tobacco smoke was associated to higher risk of hyperactivity/inattention problems in school-age children (Rückinger et al., 2010; Tiesler et al., 2011), and indoor levels of NO_2 and gas appliances were suggested to have an adverse relation with cognition at the ages of 2 and 4 (Sunyer et al., 2010; Vrijheid et al., 2012).

In addition to these indoor factors, exposure to indoor bio-contaminants might be related to mental health indicators. The Large Analysis and Review of European Housing and Health Status (LARES) study found an association between indoor mould and dampness with depression in adults (Shenassa et al., 2007), and previous studies performed in the UK observed increased prevalences, although not always statistically significant, of depressed mood in adults and children living in damp or mouldy houses, compared to those living in dry houses (Martin et al., 1987; Platt et al., 1989). Moreover, a cohort study in Poland observed that persistent exposure to mould was associated to poorer cognitive function in school age children (Jedrychowski et al., 2011).

Exposure to household microbial agents from visible mould, dampness, pets and other housing conditions (Sordillo et al., 2011) stimulates the immune system (Douwes et al., 2000; Radon, 2006; Wong et al., 2006). And the elevated blood levels of inflammatory mediators are associated with mood disorders according to several studies in animal models and human adults (Larson and Dunn, 2001; Howren et al., 2009), suggesting inflammation contributes to the development of depressive symptoms (DellaGioia and Hannestad, 2010). Moreover, animal studies found evidence that neurotoxicity could be an adverse effect of repeated airborne exposures to mycotoxins from black mould (Corps et al., 2010), and that this effect could be potentiated by bacterial polysaccharides coexposure (Islam et al., 2007).

To date, only the study by Jedrichowsky et al. assessed the effects of long-term indoor microbial exposures on mental health in children, their focus was on mould and cognitive development. Therefore, we aimed to assess the effects of the exposure to indoor factors associated with increased fungal and bacterial compounds exposure (visible mould, dampness and pet ownership) on behavioural problems in children aged 10 years, participating in two large birth cohorts in Germany.

Materials and methods

Study design and participants

The study population consisted of two ongoing population based birth cohorts conducted in Germany: The influence of life-style factors on the development of the immune system and allergies in East and West Germany PLUS the influence of traffic emissions and genetics study (LISAplus), and the German infant study on the influence of nutrition intervention PLUS environmental and genetic influences on allergy development study (GINIplus). Both studies followed the same inclusion and exclusion criteria, only healthy full-term neonates with a gestational age >37 weeks were recruited. Written informed consent was obtained for all participants and the study was approved by the local ethics committees in each participating region.

Briefly, for LISAplus, the parents of neonates admitted to maternity hospitals in Munich, Leipzig, Wesel and Bad Honnef, Germany, were contacted. A total of 3097 healthy full-term neonates were recruited in the study between December 1997 and January 1999. Screening, recruitment and exclusion criteria were described elsewhere (Heinrich et al., 2002; Zutavern et al., 2006).

The GINIplus study was designed to study the influence of nutrition intervention in infancy, environmental exposures and genetic factors on the development of allergies. Between September 1995 and June 1998, a total of 5991 healthy full-term infants born in Munich and Wesel (Germany) were recruited for the GINIplus study. A description of the study design has been published previously (Filipiak et al., 2007; Chen et al., 2009).

A total of 5078 (56% of the recruited participants) children were followed until the age of 10 years, 1761 (34.7%) in LISAplus and 3317 (65.3%) in GINIplus birth cohorts. SDQ scores were obtained for 4860 children, 1654 in LISAplus and 3206 in GINIplus. Children in LISAplus were not different from children in GINIplus regarding most characteristics. Children included in the study were not different from those not included regarding most characteristics, although participants had a higher parental educational level in both birth cohorts ($p < 0.05$).

The strengths and difficulties questionnaire

The SDQ (Goodman, 1997; Goodman et al., 1998; Woerner et al., 2002, 2004) is an internationally disseminated and validated screening questionnaire to assess mental and behavioural strengths and difficulties in 3- to 16-year-olds. The dimensions "emotional symptoms", "conduct problems", "hyperactivity/inattention", "peer relationship problems" and "prosocial behaviour" are measured by five SDQ items each, resulting in 25 items total. Every item (for example: "many worries, often seems worried.") can be rated on a three-point scale: "not true" (0), "somewhat true" (1) and "certainly true" (2). Positively worded items are reverse-scored. For each of the five scales, a sum of the ratings of the corresponding five items is calculated. The "total difficulties" score is a summary score for all scales except "prosocial behaviour". Hence, the scores for the five scales range between 0 and 10 and the "total difficulties" score takes values between 0 and 40. In the present study, we analysed the "total difficulties" score and the four dimensions included in this score. The scores were categorised according to cutoff points recommended for German samples (Woerner et al., 2004) to identify children with "normal", "borderline" or "abnormal" behaviour, and dichotomised into: "normal" and "borderline or abnormal" for the analyses.

Microbial exposure related indoor factors: visible mould, dampness and pet ownership

Questions on the indoor factors assessed in the present study were taken from questionnaires administered to the parents from birth to the child's age of 10 years. Exposure to visible mould and to dampness was reported by the parents at years 0, 1, 4, 6 and 10 in LISAplus and at years 1, 6 and 10 in GINIplus. We calculated two new variables, one for each indoor factor, including the exposures during the whole study period with two categories each: "never" and "ever". Children included in the "never" group where those whose parents reported not to have visible mould or not to have dampness at home in all the surveys. Meanwhile, children classified as "ever" were those of mothers who answered they had visible mould or dampness in at least one of the surveys. Children with no positive answers and at least one missing answer in any survey

Table 1
Description of the prevalences of the "total difficulties" scores categories in the strengths and difficulties questionnaire according to the characteristics of the study population.

	Normal (n = 4252)	Borderline (n = 304)	Abnormal (n = 304)	Total (n = 4860)
	n (%)	n (%)	n (%)	n (%)
Sex				
Male	2083 (84.16)	194 (7.84)	198 (8.00)	2475
Female	2169 (90.94)	110 (4.61)	106 (4.44)	2385
Parental education				
Low	235 (79.93)	26 (8.84)	33 (11.22)	294
Medium	1065 (84.32)	90 (7.13)	108 (8.55)	1263
High	2772 (89.71)	172 (5.57)	146 (4.72)	3090
Region				
Munich	2227 (87.33)	157 (6.16)	166 (6.51)	2550
Leipzig	338 (85.79)	31 (7.87)	25 (6.35)	394
Bad Honnef	181 (90.95)	9 (4.52)	9 (4.52)	199
Wesel	1506 (87.71)	107 (6.23)	104 (6.06)	1717
Cohort				
LISA	1441 (87.12)	114 (6.89)	99 (5.99)	1654
GINI	2811 (87.68)	190 (5.93)	205 (6.39)	3206
Mould				
Never	1948 (89.07)	123 (5.62)	116 (5.30)	2187
Ever	1941 (86.08)	152 (6.74)	162 (7.18)	2255
Dampness				
Never	3650 (88.51)	243 (5.89)	231 (5.60)	4124
Ever	370 (81.86)	32 (7.08)	50 (11.06)	452
Pets				
Never	1898 (90.17)	104 (4.94)	103 (4.89)	2105
Ever	2038 (85.20)	172 (7.19)	182 (7.61)	2392
Type of pet				
Never	1898 (90.17)	104 (4.94)	103 (4.89)	2105
Ever dog and/or cat	1414 (84.42)	128 (7.64)	133 (7.94)	1675
Ever other pets	624 (87.03)	44 (6.14)	49 (6.83)	717
Moment of first exposure to pets				
Never	1898 (90.17)	104 (4.94)	103 (4.89)	2105
Early life (0–2 years)	312 (83.65)	25 (6.70)	36 (9.65)	373
Pre-school (3–6 years)	1161 (85.12)	105 (7.70)	98 (7.18)	1364
School (7–10 years)	565 (86.26)	42 (6.41)	48 (7.33)	655

in the visible mould or in the dampness questions were excluded from the analyses.

Information on having pets at home was obtained from several questions on specific pets ownership recorded each year, from birth to 10 years old, in both cohorts. We followed the same procedure as described for mould to create a dichotomous variable ("never" and "ever"). Type of pet was a 3 categories variable created following the same procedure but discriminating between dog and/or cat ownership and other pets ("never", "ever dog and/or cat", and "ever other pets"). Furthermore, we computed a new variable according to the moment of the first pet ownership that had four categories: "never", "early life (0–2 years old)", "pre-school (3–6 years old)", and "school (7–10 years old)".

Potential confounders

In addition, other potential confounders were considered in the present study. Information on the sex of the child, study region, parental education, maternal age at birth, and having older siblings was obtained through a general questionnaire administered to the mothers at birth. Time spent in front of the television or computer was recorded as hours per day at the age of 10 years. Environmental tobacco smoke (ETS) variable was computed as a 4 category variable with data of maternal smoking during pregnancy and anybody smoking at home during the first 10 years of life. Exposure was categorised in: never exposed, only pre-natal exposure, only post-natal exposure, and pre- and post- natal exposure.

Statistical analyses

Descriptive statistics of the study population and the exposure to the indoor factors included frequencies and percentages. Crude associations were evaluated using Chi square test. Crude odds ratios (OR) and their 95% confidence intervals (CI) were obtained by logistic regressions.

Multivariable logistic and multinomial regression models were developed for the "total difficulties" score and the four subscales ("emotional symptoms", "conduct problems", "hyperactivity/inattention", and "peer relationship problems"), as dichotomous variables ("normal" and "borderline or abnormal"), and in the three categories ("normal", "borderline", and "abnormal"). Adjusted OR and their 95% CI for each exposure were obtained at three different levels of adjustment (I, II, and III): adjustment I was basic adjustment for cohort, and region; adjustment II added sex, parental education, child age at the day of the SDQ administration, maternal age at birth, time spent in front of the TV, older siblings, asthma, environmental tobacco smoke, and single mother; and adjustment III added the assessed indoor factors (and visible mould, dampness, and pet ownership). Type of pet and moment of first exposure to pets were also included in the models. Adjusting variables, excluding the exposure variables, were included in the models if they had a p-value below 0.2. Sensitivity analyses were performed stratifying by parental education and by dampness. Statistical analyses were conducted with STATA SE 10.0 statistical software (Stata Corporation, College Station, TX, USA).

Results

The population characteristics are briefly described in Table 1. According to the "total difficulties" score of the SDQ, 6.25% of the children were classified as borderline, and 6.25% as abnormal. Regarding each of the dimensions included in this score, 7.61% were classified as borderline and 10.31% as abnormal in the "emotional

Table 2
Description and adjusted associations for the "total difficulties" scores and the four studied dimensions of the SDQ, for visible mould, dampness, and pet ownership (n = 4860).

	Normal	Borderline or abnormal	Adj I[a]	Adj II[a]	Adj III[a]
	n (%)	n (%)	OR (95%CI)	OR (95%CI)	OR (95%CI)
Total difficulties					
Mould					
Never	1948 (89.07)	239 (10.93)	1	1	1
Ever	1941 (86.08)	314 (13.92)	1.30 (1.09–1.57)	1.23 (1.00–1.52)	1.19 (0.94–1.50)
Dampness					
Never	3650 (88.51)	474 (11.49)	1	1	1
Ever	370 (81.86)	82 (18.14)	1.69 (1.31–2.19)	1.51 (1.10–2.07)	1.41 (1.01–1.98)
Pets					
Never	1898 (90.17)	207 (9.83)	1	1	1
Ever	2038 (85.20)	354 (14.80)	1.61 (1.34–1.94)	1.48 (1.20–1.84)	1.55 (1.23–1.94)
Emotional symptoms					
Mould					
Never	1847 (50.64)	341 (15.55)	1	1	1
Ever	1800 (49.36)	455 (20.18)	1.38 (1.18–1.61)	1.39 (1.16–1.66)	1.40 (1.16–1.69)
Dampness					
Never	3418 (90.59)	707 (17.12)	1	1	1
Ever	355 (9.41)	97 (21.46)	1.33 (1.04–1.69)	1.23 (0.93–1.63)	1.05 (0.78–1.41)
Pets					
Never	1767 (47.83)	338 (16.06)	1	1	1
Ever	1927 (52.17)	465 (19.44)	1.27 (1.09–1.48)	1.3 (1.09–1.56)	1.27 (1.05–1.53)
Conduct problems					
Mould					
Never	1670 (76.36)	517 (23.64)	1	1	1
Ever	1655 (73.39)	600 (26.61)	1.18 (1.03–1.36)	1.11 (0.94–1.30)	1.08 (0.91–1.28)
Dampness					
Never	3115 (75.53)	1009 (24.47)	1	1	1
Ever	318 (70.35)	134 (29.65)	1.28 (1.04–1.59)	1.13 (0.88–1.47)	1.11 (0.85–1.46)
Pets					
Never	1623 (77.10)	482 (22.90)	1	1	1
Ever	1743 (72.87)	649 (27.13)	1.28 (1.12–1.47)	1.20 (1.03–1.41)	1.20 (1.02–1.42)
Hyperactivity/inattention					
Mould					
Never	1913 (87.47)	274 (12.53)	1	1	1
Ever	1926 (85.41)	329 (14.59)	1.19 (1.00–1.42)	1.07 (0.87–1.31)	1.05 (0.84–1.31)
Dampness					
Never	3595 (87.17)	529 (12.83)	1	1	1
Ever	377 (83.41)	75 (16.59)	1.36 (1.04–1.78)	1.24 (0.90–1.71)	1.25 (0.89–1.76)
Pets					
Never	1872 (88.93)	233 (11.07)	1	1	1
Ever	2024 (84.62)	368 (15.38)	1.46 (1.22–1.74)	1.24 (1.01–1.52)	1.31 (1.05–1.62)
Peer relationship problems					
Mould					
Never	1852 (84.68)	335 (15.32)	1	1	1
Ever	1870 (82.93)	385 (17.07)	1.15 (0.98–1.35)	1.06 (0.88–1.28)	1.06 (0.87–1.29)
Dampness					
Never	3492 (84.68)	632 (15.32)	1	1	1
Ever	368 (81.42)	84 (18.58)	1.25 (0.97–1.61)	1.22 (0.91–1.65)	1.13 (0.82–1.56)
Pets					
Never	1793 (85.18)	312 (14.82)	1	1	1
Ever	1987 (83.07)	405 (16.93)	1.19 (1.01–1.39)	1.16 (0.96–1.40)	1.17 (0.96–1.42)

OR (95%CI), odds ratio and 95% confidence intervals.

[a] Adj I, adjusted for cohort and region; Adj II, adjusted for Adj I and sex, parental education, child age at the day of the SDQ administration, maternal age at birth, time spent in front of the TV, older siblings, asthma, environmental tobacco smoke, and single parent; and Adj III, adjusted for Adj II and visible mould, dampness, and pet ownership.

symptoms" dimension; the borderline and abnormal percentages were 13.31% and 11.81%, respectively, for the "conduct problems" dimension; 5.31% and 8.15%, respectively, for the "hyperactivity/inattention" dimension; and 7.24% and 8.70%, respectively, for the "peer relationship problems" dimension. Regarding the indoor factors, visible mould and pet ownership were reported in half of the homes, meanwhile dampness was reported by 10% of the parents.

Table 2 shows the description of the indoor factors according to the "total difficulties" and each of the four dimensions in two categories: "normal" and "borderline or abnormal", and the associations at three different levels of adjustment (I, II, and III). The detailed adjustment did not substantially change the effect estimates for none of the indoor factors. The risk of borderline or abnormal scores in "total difficulties" was statistically significantly higher for children exposed to the three indoor factors, and in the "emotional symptoms" dimension for visible mould and pet ownership (p-values < 0.05). This factor also increased the risk of borderline or abnormal scores in the "conduct problems" and "hyperactivity/inattention" dimensions (p-values < 0.05). Table 3 shows the results of the same analyses in a subgroup of children with high parental education and not living in a single parent family.

Moreover, when we assessed the adjusted associations according to the type of pet (dogs and/or cats, or other pets) and the moment of first exposure to pets (early life,

Table 3
Description and adjusted associations for the SDQ and the indoor factors in children of high educated parents and not living in a single-parent family ($n = 2741$).

	Normal	Borderline or abnormal	Adj I[a]	Adj II[a]	Adj III[a]
	n (%)	n (%)	OR (95%CI)	OR (95%CI)	OR (95%CI)
Total difficulties					
Mould					
Never	1095 (92.33)	91 (7.67)	1	1	1
Ever	1198 (89.54)	140 (10.46)	1.41 (1.07–1.87)	1.35 (0.99–1.83)	1.26 (0.91–1.75)
Dampness					
Never	2146 (91.28)	205 (8.72)	1	1	1
Ever	227 (87.98)	31 (12.02)	1.39 (0.93–2.08)	1.50 (0.96–2.33)	1.35 (0.84–2.16)
Pets					
Never	1248 (92.10)	107 (7.90)	1	1	1
Ever	1088 (89.33)	130 (10.67)	1.48 (1.13–1.94)	1.80 (1.33–2.44)	1.84 (1.34–2.53)
Emotional symptoms					
Mould					
Never	1022 (86.17)	164 (13.83)	1	1	1
Ever	1089 (81.39)	249 (18.61)	1.48 (1.19–1.84)	1.50 (1.18–1.90)	1.46 (1.14–1.88)
Dampness					
Never	1985 (84.43)	366 (15.57)	1	1	1
Ever	205 (79.46)	53 (20.54)	1.43 (1.03–1.97)	1.50 (1.06–2.13)	1.26 (0.87–1.83)
Pets					
Never	1157 (85.39)	198 (14.61)	1	1	1
Ever	999 (82.02)	219 (17.98)	1.28 (1.04–1.58)	1.41 (1.11–1.78)	1.34 (1.05–1.70)
Conduct problems					
Mould					
Never	926 (78.08)	260 (21.92)	1	1	1
Ever	1018 (76.08)	321 (23.92)	1.13 (0.93–1.36)	1.09 (0.89–1.34)	1.05 (0.84–1.30)
Dampness					
Never	1816 (77.24)	536 (22.76)	1	1	1
Ever	190 (73.64)	68 (26.36)	1.18 (0.88–1.59)	1.21 (0.87–1.68)	1.19 (0.84–1.68)
Pets					
Never	1054 (77.79)	301 (22.21)	1	1	1
Ever	923 (75.78)	296 (24.22)	1.17 (0.97–1.41)	1.22 (0.99–1.50)	1.19 (0.96–1.47)
Hyperactivity/inattention					
Mould					
Never	1074 (90.56)	112 (9.44)	1	1	1
Ever	1192 (89.09)	146 (10.91)	1.16 (0.89–1.51)	1.03 (0.77–1.36)	1.00 (0.73–1.35)
Dampness					
Never	2117 (90.05)	234 (9.95)	1	1	1
Ever	230 (89.15)	28 (10.85)	1.09 (0.72–1.65)	1.08 (0.68–1.71)	1.14 (0.71–1.85)
Pets					
Never	1235 (91.14)	120 (8.86)	1	1	1
Ever	1076 (88.34)	142 (11.66)	1.39 (1.07–1.80)	1.39 (1.05–1.86)	1.42 (1.06–1.92)
Peer relationship problems					
Mould					
Never	1025 (86.42)	161 (13.58)	1	1	1
Ever	1137 (84.98)	201 (15.02)	1.12 (0.89–1.41)	1.06 (0.83–1.36)	1.03 (0.79–1.33)
Dampness					
Never	2032 (86.43)	319 (13.57)	1	1	1
Ever	217 (84.11)	41 (15.89)	1.17 (0.82–1.67)	1.31 (0.89–1.92)	1.18 (0.79–1.78)
Pets					
Never	1170 (86.35)	185 (13.65)	1	1	1
Ever	1041 (85.47)	177 (14.53)	1.12 (0.89–1.40)	1.29 (1.00–1.65)	1.27 (0.98–1.64)

OR (95%CI), odds ratio and 95% confidence intervals.

[a] Adj I, adjusted for cohort and region; Adj II, adjusted for Adj I and sex, child age at the day of the SDQ administration, maternal age at birth, time spent in front of the TV, older siblings, asthma, environmental tobacco smoke; and Adj III, adjusted for Adj II and visible mould, dampness, and pet ownership.

pre-school, or school age), we did not find any significant differences between the OR in each of the mentioned categories (Table 4).

The adjusted associations (adjustment III) for these outcomes in three categories ("normal", "borderline", and "abnormal") are shown in Fig. 1. We observed an increased risk of "abnormal" scores in the "total difficulties" score for each indoor factor: visible mould, dampness and pet ownership, although it was only statistically significant for pet ownership. Regarding the "emotional symptoms" dimension, we found visible mould and pet ownership increased the risk of abnormal scores (OR = 1.6, CI 95%: 1.2–2.0; OR = 1.4, CI 95%: 1.1–1.8, respectively). In the "hyperactivity/inattention" dimension, we observed a statistically significant increased risk of

abnormal score only for pet ownership exposure (OR = 1.3, CI 95%: 1.0–1.8).

Finally, we observed a statistically significant interaction between reported dampness and pet ownership. We performed stratified analyses according to the report of dampness in the home for pet ownership, type of pet, and moment of first exposure to pets. Adjusted association estimates for each group (no-dampness and dampness) are shown in Table 5. Most adjusted OR for borderline and abnormal in the "total difficulties" score, and the "emotional symptoms" dimension were two to four times higher in the dampness than in the no-dampness group, although differences were only statistically significant in the "emotional symptoms" dimension. Regarding the moment of first exposure to pets, the OR for

Table 4
Adjusted associations for the "total difficulties" scores and the four studied dimensions of the SDQ, type of pet, and moment of first exposure (*n* = 4860).

	Adj I[a]	Adj II[a]	Adj III[a]
	OR (95%CI)	OR (95%CI)	OR (95%CI)
Total difficulties			
Type of pet			
Ever dogs and/or cats	1.73 (1.42–2.11)	1.54 (1.22–1.94)	1.58 (1.23–2.01)
Ever other pets	1.35 (1.04–1.76)	1.36 (1.00–1.86)	1.48 (1.08–2.30)
Moment of first exposure to pets			
Early life (0–2 years)	1.85 (1.36–2.53)	1.46 (0.98–2.16)	1.52 (1.01–2.29)
Pre-school (3–6 years)	1.63 (1.32–2.01)	1.47 (1.15–1.88)	1.52 (1.17–1.97)
School (7–10 years)	1.46 (1.12–1.90)	1.52 (1.12–2.06)	1.61 (1.17–2.21)
Emotional symptoms			
Type of pet			
Ever dogs and/or cats	1.34 (1.13–1.57)	1.37 (1.12–1.66)	1.35 (1.10–1.65)
Ever other pets	1.10 (0.88–1.50)	1.17 (0.90–1.51)	1.09 (0.83–1.43)
Moment of first exposure to pets			
Early life (0–2 years)	1.40 (1.06–1.85)	1.38 (0.99–1.92)	1.29 (0.91–1.83)
Pre-school (3–6 years)	1.23 (1.03–1.47)	1.26 (1.02–1.55)	1.26 (1.01–1.56)
School (7–10 years)	1.28 (1.02–1.60)	1.37 (1.06–1.77)	1.28 (0.98–1.67)
Conduct problems			
Type of pet			
Ever dogs and/or cats	1.32 (1.14–1.50)	1.25 (1.05–1.48)	1.23 (1.03–1.48)
Ever other pets	1.18 (0.97–1.44)	1.11 (0.88–1.40)	1.15 (0.91–1.46)
Moment of first exposure to pets			
Early life (0–2 years)	1.54 (1.20–1.96)	1.22 (0.90–1.64)	1.25 (0.92–1.71)
Pre-school (3–6 years)	1.24 (1.06–1.45)	1.15 (0.96–1.39)	1.13 (0.93–1.37)
School (7–10 years)	1.23 (1.01–1.51)	1.30 (1.03–1.64)	1.34 (1.06–1.70)
Hyperactivity/inattention			
Type of pet			
Ever dogs and/or cats	1.51 (1.25–1.83)	1.23 (0.99–1.54)	1.30 (1.03–1.64)
Ever other pets	1.34 (1.04–1.72)	1.25 (0.93–1.68)	1.32 (0.98–1.79)
Moment of first exposure to pets			
Early life (0–2 years)	1.77 (1.31–2.38)	1.18 (0.81–1.72)	1.18 (0.80–1.76)
Pre-school (3–6 years)	1.49 (1.22–1.82)	1.26 (1.00–1.59)	1.35 (1.06–1.72)
School (7–10 years)	1.25 (0.96–1.62)	1.22 (0.90–1.66)	1.28 (0.94–1.76)
Peer relationship problems			
Type of pet			
Ever dogs and/or cats	1.22 (1.02–1.46)	1.18 (0.96–1.45)	1.17 (0.95–1.45)
Ever other pets	1.11 (0.88–1.40)	1.11 (0.85–1.47)	1.15 (0.87–1.53)
Moment of first exposure to pets			
Early life (0–2 years)	1.30 (0.97–1.74)	1.33 (0.93–1.89)	1.30 (0.90–1.87)
Pre-school (3–6 years)	1.17 (0.97–1.41)	1.13 (0.91–1.41)	1.13 (0.90–1.42)
School (7–10 years)	1.15 (0.91–1.46)	1.14 (0.86–1.50)	1.18 (0.89–1.56)

OR (95%CI), odds ratio and 95% confidence intervals.

[a] Adj I, adjusted for cohort and region; Adj II, adjusted for Adj I and sex, parental education, child age at the day of the SDQ administration, maternal age at birth, time spent in front of the TV, older siblings, asthma, environmental tobacco smoke, and single parent; and Adj III, adjusted for Adj II and visible mould, and dampness.

borderline and abnormal in the dampness group were higher for early life exposures (from birth to 2 years old) in the "total difficulties" scores and all the dimensions except for the "conduct problems".

Discussion

Exposure to visible mould, dampness and pet ownership, considered as potential sources of microbial exposure, during the first 10 years of life increases the risk of borderline or abnormal scores in the SDQ at the age of 10 years, even after considering several social factors as potential confounders. In particular, these three indoor factors increased the risk of borderline or abnormal scores in the "total difficulties" scale and its "emotional symptoms" dimension. Pet ownership also increased the risk of borderline or abnormal scores in the "conduct problems" and "hyperactivity/inattention" dimensions. Moreover, in the group of children with reported dampness at home, the risk of borderline or abnormal scores in the "total difficulties" scale and the "emotional symptoms" dimension for pet ownership was at least twice the risk observed in the group of children living in home without reported dampness. These findings point to a potential effect of chronic microbial exposure on children's behavioural problems, especially on emotional disorders, probably mediated through neurotoxicity and a potential activation of the inflammatory system.

Despite the existing evidence of the association between housing environment, specially mould and dampness, and depression in adults (Shenassa et al., 2007), to date, the effects of long-term exposure to indoor microbial agents in children have mainly been assessed regarding respiratory symptoms, allergy and asthma development (Douwes et al., 2006; Chen et al., 2010), and only one study assesses the effects of indoor mould exposure on school age cognitive function (Jedrychowski et al., 2011). To our knowledge, our study is the first study focusing on the potential effects of exposure to fungal and bacterial agents on children behaviour and emotional symptoms.

Clinical trials performed in healthy adults show that the acute exposure to low doses of endotoxin cause transient emotional symptoms, and that these symptoms take place in concordance with the increased levels of cytokines in blood (Reichenberg et al., 2001; Eisenberger et al., 2010). Furthermore, studies in patients with cancer or cardiovascular diseases observe that emotional
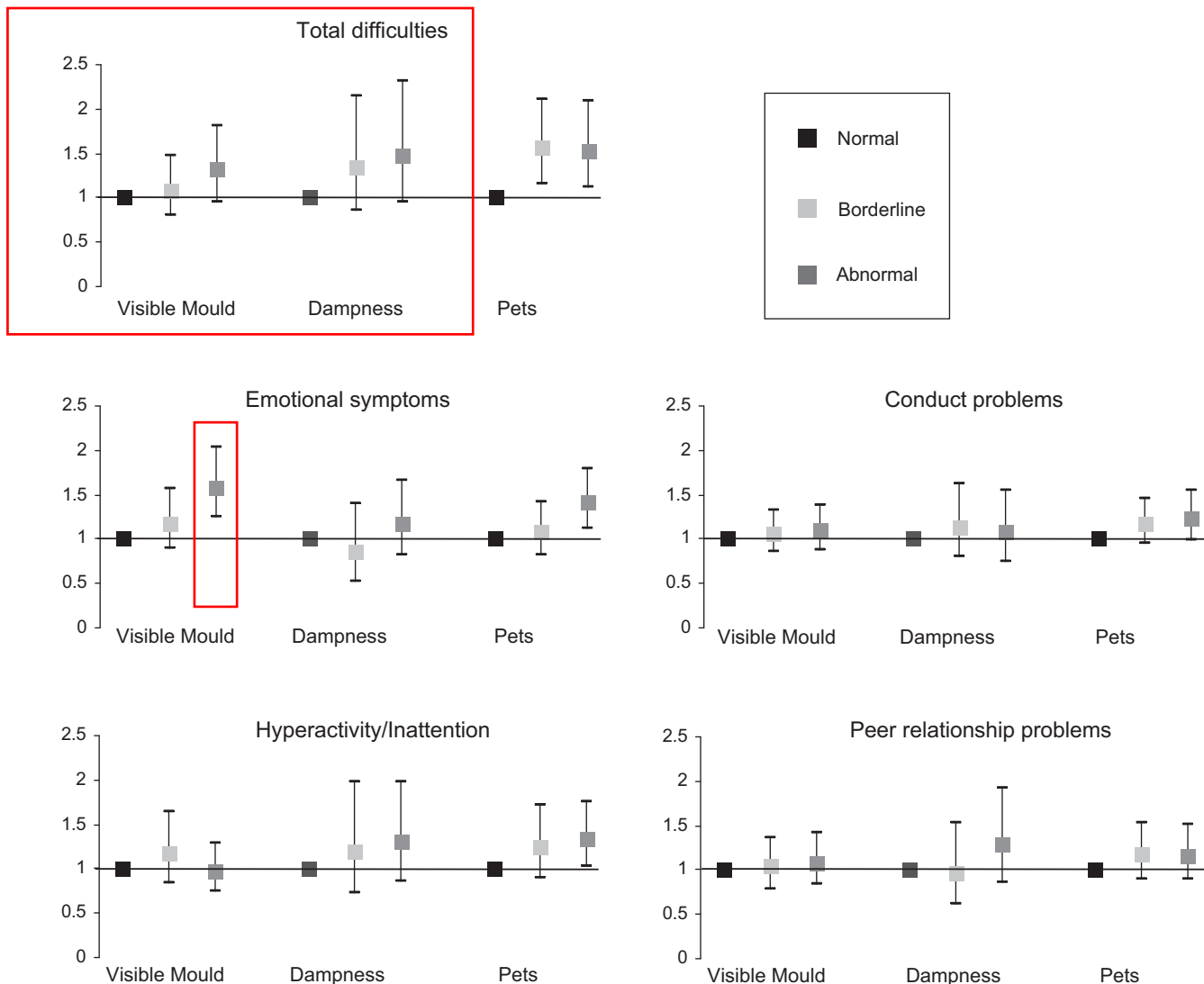
Fig. 1. Adjusted odds ratios and 95% confidence intervals for indoor factors (visible mould, dampness and pet ownership) and SDQ total difficulties scores and the four scales: emotional symptoms, conduct problems, hyperactivity/inattention, and peer relationship problems. Associations adjusted for cohort, region, sex, parental education, child age at the day of the SDQ administration, maternal age at birth, time spent in front of the TV/computer, older siblings, asthma, environmental tobacco smoke, single mother, visible mould, dampness, and pet ownership.

symptoms could be partly explained by the effects of the chronic activation of the inflammatory system (Spalletta et al., 2006; Miller et al., 2008; Pascoe et al., 2011). Besides, studies in animal models showed that repeated exposure to black mould mycotoxins is not only pro-inflammatory, but also neurotoxic. This exposure produces the loss of olfactory sensory neurons and nerve atrophy in exposed adult mice (Corps et al., 2010), and the effect is potentiated by the co-exposure to bacterial lipopolysaccharides (Islam et al., 2007).

Our results are consistent with the findings in the studies described above, although the studied population and the type of exposure in our study are different. Human central nervous system development starts during pregnancy and is still developing at the age of 10 years; therefore, the brain at this age is more susceptible to any environmental insult than at adults' age. In addition, we assess an up to 10 years exposure to three different sources of microbial agents. This could indicate we assess a very low dose and long-term exposure to indoor microbial agents.

In our longitudinal study that included two birth cohorts with participants from four different regions in Germany, data were collected following similar protocols in both cohorts. Exposure data

included in the present study were collected longitudinally in several surveys. Thus, we had repeated information on the presence or absence of each assessed indoor factor during the 10 years of follow-up. This longitudinal design allowed us to have a very well defined group of never exposed to the indoor factors. Unfortunately, for visible mould and dampness, information on the location and extend of the exposure was not obtained. Also, the family housing status (apartment ownership or lease) could make a difference in the report of mould and dampness. We may think that individuals living in a rented house may over-report water damage compared to house owners, but this information was not available in our study. As a result, we cannot exclude that some individuals with very low exposure to these two indoor factors were classified as exposed.

Moreover, we could not assess the potential reverse causation between pet ownership and behavioural problems at the age of 10 years. Although we could determine the moment of first exposure to pets at home, we did not have information on behavioural problems before the age of 10 years. Thus, we must consider the possibility that parents of children with behavioural problems in earlier ages decided to have a pet to attenuate these problems in

Table 5
Adjusted associations for the "total difficulties" scores and the four studied dimensions of the SDQ, for pet ownership, stratified by reported dampness at home.

	No dampness (n = 4124)	Dampness (n = 452)
	OR (95% CI)[a]	OR (95% CI)[a]
Total difficulties		
Pets	1.37 (1.08–1.72)	3.41 (1.62–7.21)
Type of pet		
Ever dogs and/or cats	1.44 (1.12–1.85)	2.74 (1.22–6.16)
Ever other pets	1.18 (0.84–1.67)	5.15 (2.06–12.87)
Moment of first exposure to pets		
Early life (0–2 years)	1.19 (0.76–1.85)	6.41 (1.93–21.28)
Pre-school (3–6 years)	1.41 (1.08–1.83)	2.40 (1.02–5.64)
School (7–10 years)	1.37 (0.98–1.92)	4.83 (1.86–12.57)
Emotional symptoms		
Pets	1.20 (0.99–1.45)	2.88 (1.52–5.44)
Type of pet		
Ever dogs and/or cats	1.30 (1.06–1.60)	2.40 (1.19–4.82)
Ever other pets	0.96 (0.72–1.28)	4.02 (1.80–8.99)
Moment of first exposure to pets		
Early life (0–2 years)	1.15 (0.8–1.66)	7.10 (2.36–21.33)
Pre-school (3–6 years)	1.21 (0.97–1.51)	2.29 (1.09–4.82)
School (7–10 years)	1.18 (0.9–1.57)	3.03 (1.31–6.98)
Conduct problems		
Pets	1.15 (0.97–1.37)	1.79 (1.05–3.08)
Type of pet		
Ever dogs and/or cats	1.20 (1.00–1.44)	1.50 (0.82–2.73)
Ever other pets	1.05 (0.82–1.35)	2.55 (1.24–5.24)
Moment of first exposure to pets		
Early life (0–2 years)	1.23 (0.90–1.69)	0.90 (0.29–2.85)
Pre-school (3–6 years)	1.09 (0.90–1.33)	1.70 (0.92–3.15)
School (7–10 years)	1.24 (0.96–1.58)	2.46 (1.15–5.24)
Hyperactivity/inattention		
Pets	1.24 (1.00–1.55)	1.20 (0.60–2.40)
Type of pet		
Ever dogs and/or cats	1.26 (0.99–1.60)	0.97 (0.45–2.11)
Ever other pets	1.20 (0.87–1.66)	1.75 (0.73–4.20)
Moment of first exposure to pets		
Early life (0–2 years)	0.99 (0.64–1.51)	3.14 (0.99–10.00)
Pre-school (3–6 years)	1.31 (1.02–1.68)	1.10 (0.50–2.46)
School (7–10 years)	1.26 (0.91–1.74)	0.96 (0.35–2.68)
Peer relationship problems		
Pets	1.12 (0.92–1.37)	1.67 (0.88–3.19)
Type of pet		
Ever dogs and/or cats	1.14 (0.92–1.42)	1.72 (0.85–3.47)
Ever other pets	1.08 (0.80–1.46)	1.57 (0.65–3.79)
Moment of first exposure to pets		
Early life (0–2 years)	1.22 (0.83–1.79)	3.12 (1.00–9.74)
Pre-school (3–6 years)	1.13 (0.89–1.43)	1.33 (0.62–2.85)
School (7–10 years)	1.07 (0.79–1.44)	1.98 (0.83–4.73)

OR (95%CI), odds ratio and 95% confidence intervals.

[a] Adjusted for cohort, region, sex, parental education, child age at the day of the SDQ administration, maternal age at birth, time spent in front of the TV, older siblings, asthma, environmental tobacco smoke, and single parent.

their child. However, the results for pet ownership in the "total difficulties" scale and "emotional symptoms" dimension are consistent with the results for mould and dampness, and reverse causation is not plausible for these two exposures.

In addition, the higher risk of behavioural problems related to pet ownership in children living in a damp environment, points to a biological explanation of the results. Pet ownership contributes to the total amount of house dust bacteria compounds (Heinrich et al., 2002; Giovannangelo et al., 2007), and dampness facilitates mould growth. Thus, the co-exposure to both indoor factors could potentiate the neurotoxic and pro-inflammatory effects (Islam et al., 2007; Cui et al., 2009; Schwarz and Bilbo, 2011), explaining the interaction observed between reported dampness and pet ownership, and the consequent effect modification. Furthermore, when we considered the moment of first exposure to pets we observed the risk in damp homes was higher if the exposure started during early life (from

birth to 2 years old), meanwhile differences in the risks according to the moment of exposure were not found in the not damp homes group. Since the detection of behavioural problems is not likely to occur before the age of 2 years, reverse causation in this case would not be plausible.

The main limitation of our study is the instrument used for the assessment of behavioural problems in children. The SDQ is not a diagnostic instrument but only a screening test administered to the parents that shows their own perception of their child's behavioural problems. An objective measurement of this parental perception such as a specialist evaluation of the child in the dwellings or the doctor diagnosed behavioural problems would have complemented and strengthened the results of this screening instrument. Unfortunately, that was not feasible in our study. Nevertheless, the German version of the SDQ has been found to be a reliable and valid screening instrument (Becker et al., 2004; Rothenberger et al., 2008). Furthermore, the strength of the SDQ relies on the fact that it gives equal amount of information on behavioural problems in all socio-economic status groups. According to Froehlich et al. (2007), children of parents with low socio-economic status are more likely to be infra-diagnosed of behavioural problems because of a potential differential access to health care. Moreover, the prevalences of abnormal or borderline in our study were similar to those observed in the German BELLA study, in the population aged from 7 to 10 years.

Moreover, socio-economic status, home environment, parental intelligence and parental education are important issues to consider when assessing behavioural problems in children. In our study, we only had information on the parental education and the single or not single-parent family. We observed that the prevalences of borderline and abnormal scores in the SDQ were higher in the groups of children with parents reporting lower educational levels. However, sensitivity analyses in a subgroup of children with high parental education and not living in a single-parent family did not show significant changes in the association estimates.

In conclusion, exposure to visible mould, dampness, and pet ownership, considered as potential sources of indoor microbial agents, increases the risk of behavioural problems at the age of 10, in particular, the risk of emotional problems, and this association could be mediated by the neurotoxic and pro-inflammatory effects of the microbial agents. Further investigation is required to confirm the results in our study.

Immunology/Core Facility Studies, Leipzig (Lehmann I, Bauer M, Gräbsch C, Röder S, Schilde M); University of Leipzig, Institute of Hygiene and Environmental Medicine, Leipzig (Herbarth O, Dick C, Magnus J); IUF – Institut für Umweltmedizinische Forschung, Düsseldorf (Krämer U, Link E, Cramer C); Technical University Munich, Department of Pediatrics, Munich (Bauer CP, Hoffmann U); and ZAUM – Center for Allergy and Environment, Technical University, Munich (Behrendt H, Grosch J, Martin F).

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