

# Neuropsychological effects of chronic low-dose exposure to polychlorinated biphenyls (PCBs)

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# Abstract

## Background

Exposure to indoor air of private or public buildings contaminated with polychlorinated biphenyls (PCBs) has raised health concerns in long-term users. Despite the fact that there is a lack of studies on chronic effects on nervous system functions in adults, some authors concluded that no acute or chronic health effects exist at background levels in the general population. This neuropsychological group study investigated the potential adverse effects of chronic low-dose exposure to air-borne PCB on well-being and behavioral measures in adult humans.

## Methods

Thirty employees exposed to indoor air contaminated with PCBs from elastic sealants in a school building were compared to 30 non-exposed controls matched for education and age, controlling for gender (age range 37-61 years). PCB exposure was verified by internal and external exposure data. Subjective complaints, learning and memory, executive function, and visual-spatial function was assessed by standardized neuropsychological testing. Since exposure status depended on working hours in contaminated rooms, an objectively exposed subgroup (N=16) was identified (PCB 28 $\geq$ 0.20  $\mu\text{g/l}$ ; weighted exposure duration 17.9 $\pm$ 7 years, range 4-25 years) and compared with 16 paired controls.

## Results

Blood analyses indicated a moderate exposure effect size relative to expected background exposure for the sum of PCBs (4.45 $\pm$ 2.44  $\mu\text{g/l}$ ). A significant increase was found for low chlorinated, nonplanar PCBs (PCB 28: 0.28 $\pm$ 0.25  $\mu\text{g/l}$ ,  $d=1.5$ ; PCB 101: 0.07 $\pm$ 0.09  $\mu\text{g/l}$ ,  $d=0.7$ ) whereas PCB 138, 153 and 180 were not elevated. No neuropsychological effects were observed in the total group which exceeded the corrected significance level. However, estimation statistics showed elevated effect sizes in an objectively exposed subgroup suggesting a trend towards increased subjective attentional and emotional complaints (tiredness and slowing of practical activities, emotional state) as well as attenuated attentional performance (response shifting behavior and alertness in a cued reaction task).

## Conclusions

Although neuropsychological effects of chronic exposure to air-borne PCBs could not be demonstrated on a corrected significance level, this exploratory group study showed elevated effect sizes for discriminative congeners as well as for subjective and behavioral measures of frontostriatal brain functions in adults.

## Background

Polychlorinated biphenyls (PCBs) have been used as a component of insulation fluids, paints, softening agents in lacques, glues and sealing compounds. Although banned by law in 1979 by the US Environmental Protection Agency and by many other countries, low-level presence of PCBs has been discovered in many industrial settings in the USA and worldwide (for a review, see Ross, 2004). Due to the ubiquitous presence and poor degradation of PCBs, public health concerns continue to exist. Despite the fact that few studies and no conclusive evidence is available on nervous system effects in adult humans, it has been concluded that no such acute or chronic effects exist at background levels in the general population (Ross, 2004). This study was designed to explore subtle neurobehavioral effects in the context of a neuropsychological group study and to provide information that might be relevant for the preparation of large scale epidemiological studies.

PCBs represent mixtures of up to 209 isomers and structurally related congeners differing by degree of chlorination (Hutzinger, Safe & Zitko, 1974). These can be classified with respect to their similarity to TCDD (e.g., Safe, 1994; Safe & Goldstein, 1989; Kafafi et al., 1993). Accordingly, PCBs have been categorized as (1) coplanar, non-ortho-substituted, dioxin-like PCBs (IUPAC-Nr. 77, 126, 169), (2) mono-ortho-substituted (weakly dioxin-like PCBs), and (3) nonplanar, ortho-substituted (dioxin-unlike) PCBs (Nr. 28, 52, 101, 138, 153, 180 and others).

Most frequently detected congeners in the US population were PCB 105, 118, and 156 (CDC, 2003). Major exposure routes in humans include inhalation, food intake and skin contact (for reviews see, e.g., Fischer et al., 1998; Safe & Goldstein, 1989; Tilson & Kodavanti, 1998). Indoor air of contaminated private or public buildings has been identified as a source of exposure (Gabrio et al. 2000; Schwenk et al., 2002). Animal experiments have stressed the neurotoxic potency of PCBs (Tilson & Kodavanti, 1998). The mechanisms of PCB neurotoxicity appear to include direct cerebral effects as well as indirect steroid- and thyroid-agonistic modulation (Golden et al., 1998). Neurodevelopmental effects of perinatal PCB exposure in rats were observed mainly in the striatum, prefrontal cortex and cerebellum which also depend upon age and sex (Morse et al., 1996). Prenatally exposed rats exposed to low concentrations of mono-ortho or coplanar congeners showed specifically reduced LTP in the hippocampus (Niemi et al., 1998). Changes in several neurotransmitter systems involving dopamin- and serotonin-antagonistic effects have been reported (Mariussen et al., 1999, 2001; Morse et al., 1996).

Perinatal exposure to nonplanar PCB has been associated with dopamin-antagonistic effects, whereas exposure to coplanar PCB showed dopamin-agonistic results (Brouwer et al., 1995; Seegal, Brosch & Okoniewski, 1997). Despite the fact that mono-ortho-substituted and nonplanar PCBs possess lower TCDD-toxicity equivalents (I-TEQ), some studies ascribed a greater neurotoxic potency to these substances as compared to coplanar PCB (Fischer et al., 1998; Shain, Bush & Seegal, 1991).

Alterations in human behavior, cognition, emotion and personality as a consequence of acute or chronic exposure to chlorinated hydrocarbons have been extensively investigated in the context of neuropsychological toxicology (Hartman, 1995; Niesink et al., 1999). There has been a growing interest in the neurobehavioral effects of PCBs, in particular with respect to its teratogenic and neuro-developmental toxicity in children (Brouwer et al., 1995; Fein et al., 1984; Jacobson et al., 1984, 1985;

Jacobson, Jacobson & Humphrey, 1990; Patandin et al., 1999; Walkowiak et al., 2001; Weisglas-Kuperus, 1998).

Developmental retardation involving visual memory and motor disorders has been found in children with placental-mediated PCBs (Jacobson & Jacobson, 1996; Rogan et al., 1986). Developmental studies in children up to seven years born to mothers exposed to cooking oil contaminated with PCBs and its thermal degradation products during pregnancy showed developmental delays, as measured by parental report, neurological examination and cognitive tests. This delay was seen at all ages and persisted over time (Yu et al., 1991). Four-year-old children prenatally exposed to PCBs showed more errors in short-term memory scanning and less efficient visual discrimination processing and children with the highest PCB exposure showed reduced intelligence at a later age (Jacobson & Jacobson, 1996).

Negative correlations were found for psychomotor but not for cognitive variables (Gladen & Rogan, 1991; Rogan et al., 1986; Rogan & Gladen, 1991; Tilson, Jacobson & Rogan, 1990). Other studies did not show correlations with visual memory performance (Koopman-Essebohm et al., 1996; Huisman et al., 1995ab). A prospective study found a negative relation of PCB in mother's milk and mental and motor development for all postnatal observations (Walkowiak et al., 2001). These postnatal effects are most likely associated with the prenatal exposure status of mothers (Jacobson & Jacobson, 2001).

Although a considerable body of research has studied PCB effects in young children, the information available on long-term neurobehavioral consequences in adult humans is still sparse and conclusive results are not available. Acute PCB intoxication by contaminated food was associated with subjective complaints such as fatigue, headache, dizziness, muscle weakness and memory and concentration problems as well as altered electrophysiological parameters indicating peripheral neuropathy and reduced neural velocity (Chia & Chu, 1984, 1985; Rogan & Gladen, 1992).

Consumption of PCB contaminated fish was associated with memory and learning impairment in older adults (Schantz et al., 2001).

Contaminated indoor air has been identified as another source of chronic PCB exposure. Potential long-term health effects in school and office buildings where elastic sealants containing technical PCB mixtures were used have recently been discussed (Benthe et al., 1992; Burkhardt et al., 1990; Gabrio et al. 2000; Köppl & Piloty, 1993; Neisel et al., 1999; Schwenk et al., 2002).

The present study was initiated after exposure to indoor air-borne PCBs in public school buildings has raised strong health concerns among user groups. Exposure measures related to these sites have recently been published (Gabrio et al., 2000). One of these schools was selected to objectively assess potential health complaints in employees and, further, to evaluate behavioral and cognitive effects. The purpose of the study is exploratory due to the lack of neurobehavioral investigations on PCB effects in adult humans. We first tested the global hypothesis that a difference in neurobehavioral performance between exposed subjects and controls exists. The above findings suggest subtle dysfunctions of executive, that is, frontostriatal functions that could be associated with the specific, dopamin-antagonistic effects of nonplanar PCBs. This assumption was evaluated by considering the effect sizes of performance differences.

## Methods

The present study was initiated after PCB-contaminated elastic sealant material was detected in a school building and indoor air concentrations of up to 10.655 ng/m<sup>3</sup>

were measured. The school was closed for renovation and employees were immediately submitted to a surveillance procedure which also included neuropsychological testing. All subjects underwent a medical examination including history of medical and psychosocial life events, environmental risk factors and dietary habits. The medical assessment was followed by a neuropsychological examination. An identical procedure was carried out in matched controls employed by an uncontaminated secondary school. All neuropsychological investigations were performed in the morning using an uncontaminated environment. Blood samples were drawn prior to the test session on a different occasion.

### **Study population**

60 teachers and employees of two high schools near Heidelberg, Germany, were investigated. Thirty subjects who were chronically exposed to air-borne PCBs at their workplace were compared to 30 controls with no work-related PCB exposure. Subjects were matched for education, age and professional status, controlling for gender (see Table 1). The mean age was 49.2 years (SD=7 years, range 37-61 years), with no differences between the PCB-group (48.2 years, SD=7 years, range 39-60 years) and controls (49.9 years; SD=7 years, range 37-61 years). The exposure group included 12 women, whereas controls encompassed 18 women. Although this difference of gender distribution was not statistically significant ( $\chi^2(1)=1.67$ ;  $p=.20$ ), gender was controlled for as a potential confounder. Since gender had no effect on the present PCB exposure variables (Gabrio et al., 2000) and gender effects on behavior were relatively small, a strong confounding effect is unlikely. Nevertheless, the reported means and statistics given in the Tables were statistically adjusted for gender. In the re-analysis of the data, an objectively exposed subgroup ( $>$  PCB 28 median  $0.20 \mu\text{g/l}$ ) was identified and compared with a non-exposed control group which was matched for age, education *and* gender.

(Insert Table 1 about here)

The profile of vocational activities of the two populations of employees was comparable (number of occupational years: PCB:  $20.9 \pm 6$  years, controls:  $22.0 \pm 9$  years; weekly working hours at school: PCB:  $24.6 \pm 6$  h; controls:  $24.3 \pm 9$  h). The exposed group spent  $4.2 \pm 4$  years of their vocational life outside and  $16.7 \pm 7$  years within the contaminated school building (range 1–25 years). Assuming 40 weeks working time per year, the mean weighted exposure duration was  $10.5 \pm 6$  years. According to their history, laboratory tests and a medical examination, pathological conditions of the nervous system could be ruled out. Subjects had no history of neurological or psychiatric disorders. 77% of all subjects did not take any medication; 5% of the total group reported taking drugs for allergies, hypertonia or hypothyreosis, but no drugs with substantial cerebral side effects. Physical measures were within normal limits (BMI: PCB  $T=54.9 \pm 3.5$ ; controls  $T=52.0 \pm 5.0$ ; n.s.) and an increase or decrease of body weight was not reported. Alcohol and nicotin consumption was moderate and did not differ between groups (Table 1).

### **External exposure**

Contamination by PCBs was determined by chemical analysis of indoor air and of elastic sealant materials. External exposure was determined by commercial institutes, analyzed according to standard procedures and collected by the state Public Health Authority (for detailed data on indoor air PCB-concentrations of highly contaminated rooms, see Gabrio et al., 1998, 2000). These analyses showed that the sealant material

contained up to 50 percent of PCB. Indoor measurements revealed total airborne PCB concentrations of up to 17.460 ng/m<sup>3</sup>. Air concentrations in unrenovated rooms were between 2.870 ng/m<sup>3</sup> and 10.655 ng/m<sup>3</sup>.

In order to exclude other possible sources of exposure to chlorinated substances, subjects were interviewed concerning nutritional factors and life style. No differences were evident concerning wood interiors potentially treated with preservatives (PCB 50%; controls 40%;  $\chi^2(1)=0.27$ ; n.s.), leather wear PCB (60%; 47%;  $\chi^2(1)=0.67$ ; n.s.), or daily consumption of meat products (53%; 30%,  $\chi^2(1)=2.47$ ; p=.12). Consumption of fish was more frequent in controls ( $\chi^2(1)=10.15$ ; p=0.001). No previous occupations were mentioned that might indicate exposure to other toxic substances. In the PCB group, three persons might occasionally have had contact with chlorinated compounds (lab technician, joiner, plumber). One control subject had worked in a brewery, another as a lab technician. The number of chemistry teachers was comparable in both groups (PCB 33%, controls 20%). An accumulation of potential risk factors could not be confirmed for either group (PCB: 37%; controls 20%;  $\chi^2(1)=1.31$ ; n.s.) and the confounding effects of additional exposure sources appear to be irrelevant (Table 2).

(Insert Table 2 about here)

### **Biological Monitoring**

To determine the degree of internal exposure, a biological monitoring procedure was carried out. Veinous blood samples were drawn by the Public Health Unit and gas chromatographically analyzed by the state Public Health Authority using standard protocols (Gabrio et al., 2000). Due to low concentrations of low chlorinated PCBs, measurements were close to the determination threshold of the GC-ECD method. Therefore, samples were later re-analyzed using the more sensitive mass spectrometric GC-MS method thus confirming previous findings (Schwenk et al., 2002).

Since an analysis of all congeners is not feasible for technical and practical reasons, PCB burden is typically assessed by means of gas chromatographic analysis of indicator compounds such as PCB 28, 52, 101, 138, 153, and 180 (Ballschmiter & Zell, 1980; Human Biomonitoring Commission of the National Environmental Authority, 1999). In addition to internal indicators, a weighted cumulative index of exposure duration was computed as the total duration of exposure taking into account full- or part-time occupation and working days per year. Since complete information about all congeners was not available, a total toxicity index based on TCDD-toxicity equivalents could not be estimated.

### **Neurobehavioral assessment**

Standardized neuropsychological testing (Hartman, 1995) was used to assess subtle subjective and behavioral changes. Tests selection was motivated by previous findings in humans (Schantz et al., 2001) and experimental animals (frontostriatal systems and hippocampus; see Background section). Most of the tests used have been recommended by the WHO due to their known sensitivity to neurotoxic compounds (Baker & Letz, 1986) and have been integrated into current neurotoxicity batteries such as the MANS (Cassitto, Gilioli & Camerino, 1989). Computerized testing was added to increase the sensitivity of the battery in the area of executive and attentional functions. The battery is only briefly summarized here because it has been described in previous work (Peper et al., 1993, 1999). Since the obtained scores are partly

intercorrelated, all tests were grouped according to the results of preceding factor analyses of control subjects' data.

### **Self-report measures**

Subjective and emotional complaints, and personality trait measures were organized in five clusters: current mood/ emotional state, attentional and motivational state, trait emotionality and health complaints, introversion, and sociability. For each factor, aggregated scores were also computed.

*State descriptions of general physical well-being and mood.* The Q16 questionnaire (Hogstedt, Andersson & Hane, 1984) is a well-known instrument for assessing neurotoxicity related symptom descriptions in solvent-exposed workers. Furthermore, a German version of a neurotoxicity symptoms questionnaire (Chouanière et al., 1997) was used to assess current complaints that are potentially related to neurotoxicity (factor scores were aggregated corresponding to the structure of the Freiburger Beschwerdenliste-Revised, FBL-R; Fahrenberg, 1994).

*Experience of attentional and motivational state.* State descriptions of attention and motivation as experienced in daily life were assessed by a 27-item questionnaire (FEDA, Zimmermann & Poser, 1996), yielding scores for the factors motivation and drive, fatigue and slowing of practical activities, and distractibility of mental processes.

*Trait measures of general physical well-being and emotional instability.* The Freiburg Personality Inventory (FPI-R; Fahrenberg, Hampel & Selg, 2001) was used to assess the personality trait of describing frequent health complaints and emotional instability. It included the scales impaired well-being (FPI Factor SI), aggressive arousability (FPI Factor SII), poor satisfaction with life (FPI 1), arousability (FPI 5), emotional stress (FPI 7), physical complaints (FPI 8), health worry (FPI 9), and emotional instability (FPI N). Depressed affect during the previous week was assessed by the Center for Epidemiological Studies Depression Scale (CES-D), German version (ADS; Hautzinger & Bailer, 1993). Other scales loading on this factor were General health complaints (as assessed with the FBL-R) which contained scores of 10 complaint clusters such as the sum of bodily complaints (FBL11), general well-being and physical complaints (FBL1), emotional reactivity (FBL2), cardiovascular complaints (FBL3), bowels and stomach (FBL4), tension and strain (FBL6), sensory sensitiveness (FBL7), pain (FBL8), and skin problems and cold hands (FBL10).

*Introversion.* This factor included the scales introversion (FPIE), low aggression (FPI6), reserve and low openness (FPI10), as well as low achievement and work motivation (FPI3).

*Sociability.* This sociability/psychoticism factor included inhibition (FPI4), low social orientation (FPI2), motor restlessness (FBL9), head-neck irritation (FBL5).

In addition, psychosocial life stress events were assessed with a scale proposed by Sulz (1991). According to Holmes & Rahe (1967), these events were weighted yielding a sum score for stressful events during the previous two years.

### **Behavioral tests**

*General intelligence.* An estimation of the present WAIS-IQ as an overall measure of intellectual functioning was derived from the information, similarities, block design, and picture completion subtests of the Wechsler Adult Intelligence Scale (WAIS; Dahl, 1986; Tewes, 1991).

*Fluid intelligence.* This factor included fluid intelligence measures related to verbal concept formation and reasoning processes (WAIS similarities, picture completion, and digit span forward).

*Visuo-motor performance.* Visuo-motor performance was assessed by the WAIS Block design subtest.

*Concentration, alertness and speed.* Selective attention and exploration speed was assessed with the Trail Making Test parts A and B (seconds) (cf. Lezak, 1983). Alertness was measured with the Testbattery for Attentional Performance (TAP; Zimmermann & Fimm, 1993, 2000) which was established in the context of an EU Biomed project for the standardized assessment of attentional disorders in brain damaged patients (Zoccolotti et al., 2000). The TAP subtests are equivalent to the reaction tasks of current computerized neurotoxicity batteries such as the MANS (Cassitto, Gilioli & Camerino, 1989). The alertness subtest included a simple and a cued reaction time task. Subjects were requested to respond whenever a cross appeared on the screen. In one condition, 40 visual stimuli were presented, each preceded by an acoustic warning stimulus. In the other condition, the cross appeared without warning. The difference between simple and cued reaction time was used as a measure of phasic alertness.

*Working memory.* This factor included the visual span forward, visual span backward, and verbal span backward, taken from the Wechsler Memory Scale-Revised (WMS-R; Härtling et al., 2000; Wechsler, 1945). The digit symbol subtest from the WAIS was used to assess working memory, flexibility and speed (Tewes, 1991).

Moreover, the TAP-subtests working memory performance (errors), response shifting (errors), and divided attention (errors) were also associated with this factor. The *working memory* subtest required a continuous control of the information flow through short-term memory. One-digit consecutively presented numbers had to be compared continuously with the preceding-but-one number. In the *response flexibility* task, shifting of focused attention was tested by alternations between two sets of targets (letters or numbers) which were presented simultaneously and randomly, one on the left, the other on the right side of the fixation point. From one presentation to the next the target changed from letter to number and vice versa. The subject was requested to press the key on the side of the target (left or right). *Divided attention* was investigated with a dual task paradigm which was realized by a simultaneous visual/acoustic choice condition. A series of 75 matrices was presented on the screen, each for a duration of 3 s, with an inter-stimulus interval of 500 ms. A matrix consisted of a regular array of 4 x 4 dots with seven small 'x's superimposed randomly upon them. The subject was required to react whenever four 'x's formed a square. Simultaneously, the subjects listened to high and low pitched tones in regular alternation for a period of 5 min. Occasionally, a tone was followed by a tone of the same frequency to be detected.

*Learning and memory.* Verbal memory tests included the WMS-R subtest logical memory (immediate and delayed recall of stories). Visual memory scores were derived from the WMS-R visual reproductions (immediate and delayed recall of designs). Additionally, the Auditory Verbal Learning Test (AVLT) was used to assess free recall from verbal short-term and long-term memory (cf. Lezak, 1983).

*Specific frontal lobe functions.* Word fluency measures were obtained from the RWT (Aschenbrenner, Tucha & Lange, 2000) and a design fluency task (producing as many non-recurrent figures) was added.

*Psychomotor speed and attention.* The alertness, working memory, response shifting, and divided attention subtests (TAP) described above were used to assess simple and complex choice reaction time.

### **Statistical analysis**

Analyses were done with MS-Excel, SPSS 11.0 for windows (SPSS Inc., 2000) and SAS 6.12 for windows (SAS Institute Inc., 1999). ANOVAs with the factors exposure group and gender were computed. The results of univariate F-tests for the exposure effect (with means adjusted for gender) are provided in the Tables. The re-analysis included subjects with blood values above the PCB 28 median who were compared with control subjects matched in pairs.

Firstly, the following approach was applied to test the global hypothesis (cf. Peper, 1999): (a) the original  $\alpha$ -level was set to  $p=.10$  in order to control for the  $\beta$ -error (since it is inappropriate not to detect subtle differences at this stage of research; cf. Willmes, 2000); (b) a Bonferoni adjustment of the  $\alpha$ -significance level was applied (since MANOVAs could not be computed due to sample size; cf. Bortz, Lienert & Boehnke, 1990). The correction of the Bonferoni-adjustment for dependent measures as recommended by Cross and Chaffin (1982) was used, and corrected  $\alpha$  was set to  $p=0.004$ .

Secondly, effect sizes “d” were computed. It is generally accepted today that the information value in behavioral studies can best be quantified by an estimation statistics approach (Cohen, 1988; Greenwald et al., 1996). Effect sizes were derived from  $\eta^2$  of the gender adjusted group effect ( $d_1$ ). An additional effect size estimate was computed as the deviation of the empirical value from the distribution of the normative sample ( $d_2$ ). All reported d- and T-values were uniformly scaled so that elevated values of self-report-variables ( $d \geq 0.20$ ,  $T > 50$ ) indicated elevated scores or complaints; lower values in behavioral tests ( $d \leq -0.20$ ,  $T < 50$ ) indicated attenuated performance. An effect size for a behavioural measure was classified as salient, if both  $d_1$  (corresponding to the one-tailed hypothesis  $H_1: \mu_{PCB} < \mu_{CON}$ ), as well as  $d_2$  (corresponding to the specific one-tailed hypothesis  $H_1: \mu_{PCB} < 0$ ) showed the predicted attenuation at least to a moderate degree ( $d's \leq -0.20$ ) (see Cohen, 1988).

Finally, we computed correlations between exposure variables (total PCB, the indicator congener PCB 28, and weighted exposure duration) and age-corrected behavioral variables to determine dose-response relationships. Positive correlations with exposure were expected for self-report variables and inverse associations were expected for behavioral variables. In a separate analysis, the confounding effects of openness and alcohol consumption on self-report and estimated intelligence level and alcohol on behavioral measures were partialled out. Depending on distribution characteristics, the results were also verified using Spearman rank correlations.

## **Results**

### **External exposure**

External exposure measurements indicated that 5 rooms were contaminated with indoor air PCB values ranging from 1.587 to 10.655 ng/m<sup>3</sup> (mean 7.749 ng/m<sup>3</sup>) (Gabrio et al., 1998, 2000). The elastic sealant material was the primary source of exposure but walls and floors showed a similar PCB pattern. The lower chlorinated congeners 28 and 52 were responsible for about 90% of measured PCB indicator congeners. The higher chlorinated and non-ortho-substituted or mono-ortho-

substituted PCBs were of minor importance. Figure 1 shows aggregated exposure measures for contaminated rooms indicating increased PCB values for the congeners 28, 52 and 101. The school was closed and renovated; follow up measurements in renovated rooms indicated that PCB contamination had fallen below 3.000 ng/m<sup>3</sup>.

(Insert Figure 1 about here)

### **Internal exposure**

Overall PCB exposure had a low to moderate effect size ( $d=0.4-0.5$ ) relative to expected values (as derived from individual, age-group related median plasma PCB levels taken from national background exposure data; see Becker et al., 2002; Human Biomonitoring Commission of the German National Environmental Authority, 1999). This was mainly due to low chlorinated PCBs (PCB 28:  $0.28\pm 0.25$  µg/l,  $d=1.5$ ; PCB 101:  $0.07\pm 0.09$  µg/l,  $d>0.7$ ) which are known to accumulate from respiratory rather than from nutritional sources (Figure 2). In contrast, exposure to the congeners PCB 138, 153 and 180 was not elevated and most likely associated with general background exposure including food. More than 90 percent of control subjects showed PCB 28 and PCB 101 levels below detection threshold, whereas most of the exposed subjects showed detectable blood levels of these congeners ( $p<0.001$ , Fisher's exact test; see Table 1). PCB28 values were above the range of controls in 53 percent of the PCB-exposed subjects.

(Insert Figure 2 about here)

Table 2 shows the relationship of internal and external indices. Blood PCB 28 and 101 were correlated with the cumulative index on a corrected significance level. For PCB 138, 153 and 180, these correlations were not significant. An above-average fish consumption was also correlated with PCB 28. Therefore, we examined whether PCB 28 could have been modified by alternative sources of exposure. An explorative logistic regression model with stepwise variable selection was used which included demographic information as well as potential sources of exposure. A significant model for predicting blood values (which were dichotomised at the median of controls) could only be generated for PCB 28 ( $\chi^2(2)=59.5$ ;  $p<.0001$ ;  $R^2=.84$ ). The weighted exposure index significantly contributed to the explanation of variance ( $p=.005$ ). Age, alcohol and nicotine, as well as fish consumption had no strong predictive value. A similar but weaker model was found for PCB 101 ( $\chi^2(1)=19.6$ ;  $p<.0001$ ;  $R^2=.42$ ).

Thus, nutritional and other exposure sources appeared to be of minor importance for predicting the present PCB 28 blood values. In contrast, all other congener values were associated with additional risk factors such as potentially contaminated food, leather wear etc. Therefore, it was reasonable to focus dose-response analyses on PCB 28 values which were causally connected with the PCBs originating from the present elastic sealants material.

### **Self-reported health complaints**

All subjects were in a generally satisfactory healthy condition. No symptoms were observed that might indicate an acute or chronic PCB intoxication. In the self-report inventories employed, the extent of complaints did not exceed the average values of the normative sample. Diseases reported most frequently were allergies (42%), asthma and bronchitis (29%), and hypertension (16%), with no differences between both groups. Comparisons between the group of high school employees exposed to airborne PCBs with the non-exposed control group did not reveal significant group or

gender related differences in complaints associated with the cardiovascular system (PCB: 10%; controls: 20%), skeletal motor-system (10%; 17%), respiratory system (17%; 17%), allergies (27%; 23%), thyroid dysfunctions (7%; 3%), hepatitis (7%; 3%), diabetes (0%; 7%), or head ache (0%; 7%).

### **Neuropsychological results**

The global hypothesis of at least one group differences in self report or neurobehavioral variables could not be confirmed on a corrected significance level. Whereas the Q16 indicated no complaints, the Euroquest showed a trend towards reduced scores for well-being and distractibility of mental processes (Table 1). The exposed group also showed slightly elevated scores for the personality dimension of introversion. Estimation statistics indicated moderate effect sizes of group differences for the variables distractibility, low level of well-being, head-neck pain syndrome, and for the personality trait variables of introversion, social orientation and low aggression.

The behavioral results indicated average and comparable intellectual functioning in both groups (Table 3). Small, yet non-significant effects corresponding to hypothesis were found only for the TAP divided attention subtest. Moderate effect sizes were also observed for phasic alertness and Trails A. A general trend towards slightly increased reaction times in all of the computerized attentional tasks in the exposed group must be noted which, however, were within the range of the normative population. Learning and memory performance of both groups was average. Inconsistent with hypothesis, the exposed group showed better immediate and delayed visual memory performance, an effect, however, which could not be replicated by the re-analyses summarized below.

(Insert Table 3, 4 about here).

### **Dose-response-relationships**

Significant relationships of dose indicators (PCB sum, PCB 28 and cumulative index) and response measures (self report or behavior) could not be demonstrated on a corrected significance level. Self-reported complaints and mood state showed no substantial positive association with PCB or the cumulative index. For behavioral variables, however, moderate correlations were found for PCB 28. Correlations with figural fluency ( $r=-0.54$ ;  $p<.01$ ), simple reaction time ( $r=0.31$ ;  $p<.05$ ), TAP response shifting errors ( $r=-0.31$ ;  $p<.05$ ), world list learning ( $r=-0.38$ ;  $p<.05$ ) and digit symbol ( $r=-0.32$ ;  $p<.05$ ) survived a reanalysis with rank correlations and partialing out of estimated intelligence level and alcohol consumption. Mood and personality variables showed no clear association with the behavioral data.

### **Re-analysis of subgroup with elevated PCB 28 blood levels**

Since exposure status was variable due to different working habits in contaminated rooms, a re-analysis was done with objectively exposed subjects with PCB 28 levels  $\geq 0.20 \mu\text{g/l}$ . This substance was chosen as a marker because it was significantly elevated in the present sample and was correlated with the indoor air PCB burden. Two persons from the former exposure group were assigned to the control group because they had been working in the contaminated school only for a short while and showed no elevated blood values. This objectively exposed group (12 males, 4 females,  $49.8\pm 6$  years, weighted exposure duration  $17.9\pm 7$  years, range 4-25 years) and controls (12 males, 4 females,  $48.6\pm 8$  years, pairwise matched for sex, age and education) were also comparable with respect to physical characteristics and alcohol

consumption and smoking. Estimated intelligence level (IQ  $119.5 \pm 5$  and  $118.0 \pm 7$ ;  $d=0.24$ ; n.s.) was used as a covariate in the behavioral analyses.

PCB 28 levels of exposed subjects (median =  $0.30 \mu\text{g/l}$ ; range  $0.20$ - $1.05 \mu\text{g/l}$ ) were above the distribution of controls ( $> 0.01 \mu\text{g/l}$ ). Significant differences were also found for PCB 138 ( $1.453 \pm 0.59 \mu\text{g/l}$  and  $0.953 \pm 0.37 \mu\text{g/l}$ ;  $p=0.01$ ), PCB 153 ( $1.906 \pm 0.85 \mu\text{g/l}$  and  $1.272 \pm 0.47 \mu\text{g/l}$ ;  $p=0.01$ ) as well as PCB 180 ( $1.316 \pm 0.69 \mu\text{g/l}$  and  $0.725 \pm 0.25 \mu\text{g/l}$ ;  $p=0.003$ ).

The comparison of neuropsychological data did not show differences on a corrected significant level. Nevertheless, when the five factors of self-report measures were inspected, the aggregated values for attention and motivation showed a trend towards increased complaints in the PCB group ( $T=54.6 \pm 10$  and  $T=47.8 \pm 11$ ;  $p=.04$ ;  $d=0.58$ ) which were due to greater reports of tiredness and slowing just missing the corrected level ( $T=54.6 \pm 10$  and  $T=45.9 \pm 7$ ;  $p=.006$ ;  $d=0.70$ ). The exposed group also showed a trend towards elevated emotional reactivity ( $T=53.1 \pm 11$  and  $T=46.8 \pm 10$ ;  $p=0.05$ ;  $d=0.46$ ). Openness to answer questionnaires correctly was similar in both groups. Differences in behavioral variables according to hypothesis were found for attentional functions as indicated by TAP phasic alertness ( $T=45.3 \pm 12$  and  $T=48.1 \pm 14$ ; n.s.,  $d=-0.32$ ) and response shifting ( $T=45.2 \pm 15$  and  $T=50.7 \pm 9$ ; n.s.,  $d=-0.40$ ).

## Discussion

Chronic low-dose exposure to air borne polychlorinated hydrocarbons has repeatedly raised strong health concerns in subjects exposed in their everyday work environment or at home. This study supplements the available knowledge concerning potential neurobehavioral effects of chronic PCB exposure in adult persons. The results show that the global null hypothesis could not be rejected on a corrected significance level because differences between exposed subjects and non-exposed controls were relatively small and because mean normative values did not exceed the levels required for the identification of impaired persons. However, to obtain “significant” results according to traditional null hypothesis testing, a sample size of approximately 200 to 500 PCB-exposed persons would have been necessary. The effect sizes reported herein may therefore help to estimate the potential replicability in the context of broader multicenter epidemiological research approaches.

### External and internal PCB exposure

Elevated PCB values were found for low chlorinated indicator congeners such as PCB 28 which corresponds to previous findings (Gabrio et al., 2000; Schwenk et al., 2002). The additional PCB burden relative to background exposure has been estimated to 2.8% (Gabrio et al., 2000). This corresponds to an approximate PCB 28 exposure effect size of  $d=0.34$  (to include PCB 52 would result in  $d=0.54$ ). This suggests an acceptable discrimination of the present PCB 28 burden from background exposure. Nevertheless, a reliable measurement of low chlorinated compounds may have been compromised by several factors. Since unstandardized methods of analysis and measurement errors may increase the variability of PCB values close to the detection threshold, the quality of analyses has been controlled (Gabrio, 1997). Moreover, PCB 28, 52 and 101 show a relatively fast decomposition and half-life of about 60 days (Gabrio et al., 2000; Schrenk, 1994). A decrease of PCB blood values was noted after the exposure source had been removed (data not presented). Fluctuations due to individual differences in metabolism, room and ventilation conditions, etc., may have obscured dose-response relationships. Furthermore, blood PCB values may

misrepresent the concentration in other organs such as the brain where only about 10% of the blood PCB burden can be found (Beck, Mathar & Palavinskas, 1997). These factors could be responsible for an underestimation of actual dose-response relationships. However, the correlation analyses indicated that PCB 28 blood values were successfully predicted by the cumulative exposure index suggesting that these values represent an appropriate estimate of the PCB burden.

Due to the limited number of indicator congeners investigated, no information could be obtained for the more toxic PCDD/Fs or the dioxin-like non- or mono-ortho-substituted PCB 77, 126 and 169 which might also have induced neurobehavioral effects (e.g., Peper et al., 1993). Nevertheless, in a subsequently pooled blood sample analysis, a significant increase of these compounds could not be verified (Schwenk et al., 2002) suggesting that the current results are not affected by these substances.

A generalization of the present findings to conditions with unconfirmed environmental PCB exposures does not seem warranted. For example, no elevated blood values were found in 77 persons also exposed in a contaminated school building (Burkhardt et al., 1990). Inhalative exposure (up to 13.500 ng/m<sup>3</sup>) of school teachers by another contaminated school showed PCB 28, 52 and 101 values to be below 0.01 µg/l and high-chlorinated congeners 153, 138 and 180 did not differ significantly from controls (Ewers et al., 1998).

At least partial generalizations to other PCB exposure conditions or paths of incorporation might be possible. Nevertheless, due to high volatility, the low to medium chlorinated congeners PCB 28, 52 and 101 predominate in the indoor air, whereas the high-chlorinated PCB 138, 153 and 180 may prevail in contaminated food. Low chlorinated PCB fractions will be metabolised and eliminated more easily than high chlorinated compounds. A diverging PCB pattern or additional pollutants at another site may thus produce a different behavioral effect (Brouwer et al., 1995).

### **Self reported complaints and neurobehavioral performance**

Moderate effect sizes were found for distractibility, well-being, as well as for trait measures that indicated greater social orientation and low aggression. Since individual exposure status was uncertain due to different contamination levels and use of rooms, a re-analysis based upon internal exposure was performed. The results of this subgroup analysis showed a trend towards increased self-reported tiredness and slowing, and emotional reactions.

Since the degree of complaints was not correlated with PCB exposure, these self-report data appear to depend on and could be confounded by additional factors such as health concerns resulting from information about exposure. Certain personality traits have been reported to sensitize for the consequences of exposure events (e.g., Labarge & McCaffrey, 2000). In particular, perceived olfactory stimuli may influence well-being, emotional reactivity and health concerns (Dalton et al., 1997; Orbaek et al., 1998). In the present sample, however, no personality disorders or chemical sensitivities were observed.

In contrast, behavioral measures are less biased by information about exposure status. Weak to moderate effects were found for attentional measures such as alertness and response shifting. Furthermore, moderate correlations between PCB and behavioral variables was found for figural fluency, response shifting and digit symbol. These findings, however, diverge from the results of Schantz et al. (2001) who reported lower scores in learning and memory but not in executive functions. Unfortunately, the authors did not analyze their PCB congener pattern. A possible reason for the different behavioral effects might be a greater exposure of fish eaters to high

chlorinated, mono-ortho or coplanar congeners (the latter had greater developmental effects on hippocampal LTP in animals, Niemi et al., 1998). The current control subjects also reported greater consumption of fish. However, fish eating had no predictive value for nonplanar PCB blood levels in our study.

### **Behavioral effects of chronic exposure to nonplanar PCBs**

Animal studies demonstrated that certain chlorinated hydrocarbons induce dopamine depletion which could be responsible for modulated frontostriatal function. For example, nonplanar PCB – and thus PCB 28 – may produce dopamin-antagonistic effects in the striatum and prefrontal cortex (Brouwer et al., 1995; Mariussen et al., 2001; Morse et al., 1996; Seegal et al., 1997).

It is well accepted that mental flexibility, shifting the attentional focus and other executive functions are associated with dopamine-related frontostriatal activity in healthy individuals (*e.g.*, Volkow et al., 1998). Disorders of frontal brain regions may affect attentional functions, alertness and working memory (*e.g.*, McDonald, Flashman & Saykin, 2002) and mood (*e.g.*, Brody et al., 2001).

In the present study, objectively exposed persons experienced greater tiredness, slowing and emotional reactions. The involved behavioral functions – response shifting, digit symbol and figural fluency – rest upon and require contributions of the superior and ventromedial prefrontal cortex (Fellows & Farah, 2003; Konishi et al., 2003).

Therefore, the observed subjective and behavioral effects appear to be compatible with the hypothesis of a subtle attenuation of frontostriatal functions in the exposed subgroup. Nevertheless, effects were relatively small and might have been moderated by confounders such as differences between city and rural populations in life style and nutritional habits, different performance profiles associated with school type, or motivational factors.

Nevertheless, the present estimation statistics approach informs about low response effects which might lead to, for example, a loss of work efficiency or psychopathological disorders. Even low effects may induce considerable economical costs when a large population is affected across an extended time span (Peper, 2004). These environmental costs have ultimately to be borne by society.

## **Conclusions**

This exploratory study showed that the discriminative congeners typical for the present chronic exposure condition could be identified from the range of environmental PCBs. Although neurobehavioral effects could not be demonstrated on a corrected significance level, group differences with low effect sizes suggested subjective attentional and emotional complaints as well as attenuated attentional performance. These indicators point to a trend of attenuated frontostriatal function and should be explored by future studies in greater detail.

## **Competing interests**

The authors declare that they have no competing interests.

## **Authors' contributions**

MP provided all basic contributions to conception, design and methodology, performed the statistical analysis, wrote the draft version of the article and revised it critically for content. MK participated in the design and coordination, collected blood

samples, provided internal monitoring and additional medical data, and corrected the final manuscript. RM participated in the maintenance of the study, revising the article critically for important intellectual content, and providing final approval. All authors read and approved the manuscript.

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## Figures

### **Figure 1 - PCB-concentrations of indoor air**

Means of PCB measurements from three highly contaminated rooms (room 303, 407 and teacher's room) are given (Gabrio et al., 2000, Table 3, p. 1058, modified).

### **Figure 2 - Blood values of PCB-exposed and control subjects**

Blood values of the exposed and control groups (means and standard deviations) are given. Expected values were estimated for each individual subject and averaged across the exposed group. These values were determined from age-group related reference values (median PCB-plasma values for the congeners PCB-138, -153 und -180 as published by the commission "Human-Biomonitoring" of the German National Health Authority, Umweltbundesamt (1999)).

## Tables

**Table 1 - Demographic and exposure data of subjects exposed to PCB and control subjects.**

**Table 2 - Correlations of external exposure indices and internal PCB-values.**

**Table 3 - Mood, physical complaints and personality traits.**

Primary and aggregated secondary factor scores for 30 PCB-exposed and 30 control subjects.

**Table 4 - Neuropsychological results**

Behavioral data in 30 PCB-exposed and 30 control subjects sorted by factor.

## Tables

	PCB Exposure		Controls		F/[1,56]	p
	Mean	SD	Mean	SD		
Gender [N; m/f]	18/12		12/18		1,67 <sup>1</sup>	0,20
Age [a]	48,2	7	49,9	7	0,89	0,35
Education [a] <sup>2</sup>	12,5	2	12,4	2	0,03	0,86
Vocational index <sup>2</sup>	5,9	0	5,8	0	0,39	0,54
Estimated intelligence [IQ] <sup>2</sup>	117,3	5	117,3	4	0,00	0,99
Height [cm]	174	8	169	7	1,91 <sup>3</sup>	0,17
Weight [kg]	76	14	66	12	3,00 <sup>3</sup>	0,09
BMI [T-value]	54,9	4	52	5	2,21 <sup>3</sup>	0,14
<i>Self-reported data</i>						
Alcohol consumption [g/week]	94,4	76	72,4	75	1,26	0,27
Nikotin consumption [cig./d]	6,4	10	5,7	10	0,07	0,79
Q16-Score <sup>4</sup>	4,4	4	3,6	4	0,67	0,42
EQ Euroquest complaint score <sup>4</sup>	146,4	32	131,6	31	3,29	0,07
Memory and attention	27,0	6	23,9	6	3,62	0,06
Drive and motivation	23,7	6	19,7	6	6,17	0,02 *
Tiredness	25,2	6	23,0	6	1,98	0,16
Emotional reactivity	20,0	6	17,7	6	2,41	0,13
Sensory complaints	8,1	3	7,4	3	0,65	0,42
Motor complaints	5,2	2	4,8	2	0,96	0,33
Cardiovascular complaints	14,8	5	12,0	5	4,76	0,03 *
Bowel and stomach	9,7	3	10,5	3	0,96	0,33
Head and neck	11,0	4	12,3	4	1,90	0,17
Stress inventory score <sup>4</sup>	25,6	44	23,0	43	0,05	0,82
<i>Exposure indices</i>						
Σ PCBs [µg/l]	4,45	2,44	3,65	1,40	1,87	0,067
PCB-28 [µg/l]	0,28	0,25	0,016 <sup>5</sup>	0,02		0,0001 ***
PCB-101 [µg/l]	0,07	0,09	0,01 <sup>5</sup>	0		0,0003 ***
PCB-138 [µg/l]	1,29	0,69	1,13	0,46	1,44	0,16
PCB-153 [µg/l]	1,68	0,96	1,56	0,58	1,07	0,29
PCB-180 [µg/l]	1,14	0,65	0,94	0,39	1,76	0,08
Total occupational time [a]	20,9	6	22,0	9	1,09	0,28
Duration of exposure [a] <sup>6</sup>	16,7	9	n.a.			
Weighted duration of exposure [a] <sup>6,7</sup>	10,5	6	n.a.			
<sup>1</sup> $\chi^2$ [1]; *: p<.05; ***: p<.001.						
<sup>2</sup> According to Wilson et al. (1976)						
<sup>3</sup> Statistically adjusted for gender, F[1,55]						
<sup>4</sup> A greater score corresponds to a greater number of complaints						
<sup>5</sup> 95 percent < measurement threshold; median and IQR/2 is given						
<sup>6</sup> n.a.: not applicable						
<sup>7</sup> Under consideration of the mean time of presence at school.						

**Table 1. Demographic and exposure data of subjects exposed to PCB and of control subjects.**

	PCB 28		PCB 101		PCB 138		PCB 153		PCB 180		PCB Sum	
Age <sup>1</sup>	0,17		0,17		0,27 *		0,27 *		0,26 *		0,28 *	
BMI <sup>1</sup>	0,39 **		0,26 *									
Hours of work/week <sup>1</sup>	<b>0,63</b> ***		<b>0,51</b> ***		0,19				0,21		0,25 <sup>x</sup>	
PCB years of exposure <sup>1</sup>	<b>0,71</b> ***		<b>0,54</b> ***		0,37 **		0,32 *		0,39 **		<b>0,43</b> ***	
Weighted total exposure index <sup>1</sup>	<b>0,71</b> ***		<b>0,59</b> ***		0,39 **		0,33 **		0,40 **		<b>0,45</b> ***	
Alcohol/week <sup>1</sup>			0,31 *		0,27 *		0,24 <sup>x</sup>				0,22 <sup>x</sup>	
Cigarettes/day <sup>1</sup>							-0,20		-0,26 *		-0,17	
Alternative vocational sources <sup>2</sup>							0,28 *				0,18	
Leather clothing <sup>2</sup>	0,24				0,24				0,33 *		0,33 *	
Consumption of fish <sup>2</sup>	<b>0,42</b> ***		0,27 *									
Consumption of poultry <sup>2</sup>									0,19			
<i>Note.</i> Correlations with alternative exposure sources such as indoor installations of treated wood, frequent meat or milk consumption, were not significant. Those correlations which remain significant following Bonferoni-correction are printed in bold.												
<sup>1</sup> Spearman rank correlations												
<sup>2</sup> Cramer-V												

**Table 2. Correlations of external exposure indices and internal PCB-values in all subjects.**

	PCB Exposure		Controls		$F[1,56]^2$	$p$	$d_1^3$	$d_2^3$	
	Mean	SD	Mean	SD					
<b>Current emotional mood state<sup>4</sup></b>							0,41 <sup>5</sup>	0,36 <sup>5</sup>	
EQ Tiredness/Deactivation	54,3	13	50	10	2,06	0,16	0,38	0,36	Δ
EQ Emotional reactivity	53,6	11	50	10	2,41	0,13	0,41	0,33	Δ
EQ Low well-being	55,5	13	50	10	3,29	0,07 *	0,49	0,47	Δ
<b>Attentional and motivational state</b>							0,25	0,24	
FEDA Poor motivation and drive	50,4	12	48,2	11	0,55	0,46			
FEDA Fatigue and slowing	52,5	11	49,7	10	1,07	0,30	0,28	0,24	Δ
FEDA Distractability	55,0	11	48,8	10	5,26	0,03 *	0,61	0,48	Δ
<b>General physical well being and emotional instability (trait)</b>							0,02	0,21	
FPI Factor SI/ Impaired well-being	48,1	6	50,0	6	1,40	0,24	-0,32	-0,23	Δ
FPI Factor SII/ Aggressive arousability	48,3	7	52,3	7	4,44	0,04 *	-0,57		
FPI 1 Poor satisfaction with life	46,6	10	49,6	10	1,35	0,25	-0,31	-0,34	Δ
FPI 5 Arousability	50,5	12	51,8	12	0,16	0,69			
FPI 7 Emotional stress	51,9	10	51,6	10	0,01	0,92			
FPI 8 Physical complaints	46,2	9	47,3	9	0,23	0,64		-0,40	
FPI 9 Health worry	47,7	9	51,5	9	2,39	0,13	-0,42	-0,23	Δ
FPI N Emotional instability	48,4	11	47,2	11	0,16	0,69			
FBL11 Sum of bodily complaints	54,6	9	53,4	9	0,25	0,62		0,48	
FBL 1 Gen. well-being/phys. Complaints	53,9	9	49,8	9	3,22	0,08 *	0,48	0,41	Δ
FBL 2 Emotional reactivity	55,0	10	51,9	9	1,65	0,20	0,34	0,51	Δ
FBL 3 Cardiovascular complaints	53,1	9	52,3	9	0,12	0,73		0,32	
FBL 4 Bowels and stomach	53,8	8	53,9	8	0,00	0,96		0,41	
FBL 6 Tension, strain	53,2	10	52,2	10	0,17	0,68		0,32	
FBL 7 Sensory sensitiveness	56,0	9	55,2	9	0,13	0,72		0,63	
FBL 8 Pain	52,3	10	51,9	9	0,03	0,87		0,23	
FBL 10 Skin and cold hands	54,2	10	55,9	10	0,44	0,51		0,42	
ADS Depressed affect	48,0	9	47,8	12	0,01	0,94			
<b>Introversion</b>							0,45	0,35	
FPI E Introversion	54,6	11	50,4	11	2,12	0,15	0,39	0,43	Δ
FPI 6 Low Aggressivity	54,7	8	49,2	8	6,42	0,01 *	0,68	0,51	Δ
FPI 10 Reserve, low openness	50,9	11	45,7	10	3,63	0,06 *	0,51		
FPI 3 Low achievement/work motivation	52,6	9	52,5	9	0,00	0,97		0,27	
<b>Sociability</b>							0,38	0,34	
FPI4 Inhibition	52,0	11	47,9	11	2,22	0,14	0,40		
FPI 2 Low social orientation	42,9	8	47,5	8	4,45	0,04 *	-0,57	-0,77	Δ
FBL 9 Motor restlessness	54,7	9	51,4	9	1,84	0,18	0,36	0,48	Δ
FBL 5 Head-neck irritation	56,1	9	51,5	9	3,73	0,06 *	0,52	0,63	Δ
<b>Aggregated secondary factors</b>							0,30	0,26	
Current mood/ emotional state	53,6	8	50,4	8	2,25	0,14	0,40	0,40	Δ
Reduced attention and motivation	52,6	10	49,7	10	1,25	0,26	0,30	0,26	Δ
Low well being/ trait emotionality	49,3	7	50,4	7	0,42	0,52			
Introversion	53,2	6	49,5	6	5,08	0,03 *	0,61	0,38	Δ
Low Sociability	47,4	6	47,7	6	0,02	0,88		-0,31	
<sup>1</sup> T-Score; greater values correspond to elevated feature score									
<sup>2</sup> *: F-values for group with control of gender; p: significance relative to original- $\alpha$ ; Bonferoni-adjusted p's: n.s.									
<sup>3</sup> Effect sizes in comparison with controls ( $d_1$ ; with control of gender) and in comparison with normative sample ( $d_2$ ); Δ: relevance of the effect, see text.									
<sup>4</sup> T-values relative to controls									
<sup>5</sup> Median effect sizes									

**Table 3. Mood, physical complaints and personality trait measures: primary and aggregated secondary factors in 30 PCB-exposed and 30 control subjects.**

	Raw Values				T-Scores				$F[1,56]$ <sup>2</sup>	$p$	Effect sizes	
	PCB Exposure		Controls		PCB Exposure		Controls				$d_1$ <sup>3</sup>	$d_2$ <sup>3</sup>
	Mean	SD	Mean	SD	Mean <sup>1</sup>	SD	Mean <sup>1</sup>	SD				
<i>General intelligence, crystallised verbal intelligence</i>											-0,16 <sup>4</sup>	1,03 <sup>4</sup>
WAIS IQ	72,2	9	72,2	9	113,3	10	115,8	10	0,86	0,36	-0,25	1,09
WAIS General knowledge	18,2	3	17,7	3	58,2	9	58,8	9	0,07	0,79		0,97
<i>Fluid verbal intelligence</i>											0,02	1,15
WMS Digit span forward	9,7	2	9,2	2	60,0	10	57,7	10	0,79	0,38	0,24	0,99
WAIS Similarities	19,7	3	19,3	3	63,0	9	62,8	9	0,01	0,94		1,38
WAIS Picture completion	12,4	2	12,7	2	61,1	10	63,2	10	0,74	0,39	-0,23	1,15
<i>Visuo-motor performance</i>											-0,21	0,47
WAIS Block design	21,9	6	22,5	6	53,6	7	55,0	7	0,63	0,43	-0,21	0,47
<i>Concentration, alertness and speed</i>											-0,41	0,05
Trail making Test, part A	37,5	11	34,4	11	50,1	7	53,5	7	3,67	0,06*	-0,51	
Trail making Test, part B	79,3	27	74,6	27	53,7	7	55,6	7	1,11	0,30	-0,28	0,46
TAP Phasic alertness	0,024	0,1	0,058	0,1	45,9	12	50,8	12	2,34	0,13	-0,41	-0,38 <sup>Δ</sup>
<i>Working memory</i>											-0,08	0,08
WMS Visual span forward	8,5	2	8,2	2	50,7	13	50,5	13	0,00	0,95		
WMS Visual span backward	8,0	2	7,3	2	50,6	10	47,6	10	1,31	0,26	0,31	
WMS Verbal span backward	7,2	2	7,4	2	50,2	11	52,8	11	0,84	0,36	-0,25	
TAP Working memory/ errors	4,9	4	6,3	4	52,3 <sup>5</sup>	11	50 <sup>5</sup>	10	2,08	0,16	0,39	0,23
TAP Response shifting/ errors	6,3	4	6,0	4	47,5 <sup>5</sup>	14	50 <sup>5</sup>	10	0,09	0,76		-0,20
TAP Divided attention/ errors	2,0	1	1,2	1	43,5 <sup>5</sup>	10	50 <sup>5</sup>	10	4,79	0,03*	-0,58	-0,65 <sup>Δ</sup>
WAIS Digit symbol	53,3	11	54,0	11	56,3	9	57,1	9	0,12	0,73		0,61
<i>Verbal memory</i>											0,40	-0,83
WMS Logical memory immediate rec.	22,5	7	21,7	7	42,2	9	41,5	9	0,09	0,76		-0,85
WMS Logical memory delay	18,9	7	16,3	6	42,8	9	39,4	9	2,24	0,14	0,40	-0,83
AVLT Word list learning	75,8	11	70,8	11	53,8	9	49,6	9	3,08	0,08*	0,47	0,29
<i>Visual memory</i>											0,93	0,83
WMS Visual memory immediate rec.	39,5	5	34,2	5	61,7	10	52,4	10	13,26	0,001***	0,97	1,24
WMS Visual memory delay	34,2	9	27,1	9	56,3	12	46,2	12	11,09	0,002***	0,89	0,43
<i>Specific frontal lobe functions</i>											0,24	0,42
RWT Word fluency	17,2	3	16,0	3	55,3	6	53,7	6	1,19	0,28	0,29	0,69
Design fluency	30,6	7	29,3	7	51,5	9	50,2	10	0,53	0,47		
<i>Psychomotor speed</i>											-0,39	-0,24
TAP Simple reaction time (RT)	281,1	125	253,8	123	48,7	14	52,3	13	1,06	0,31	-0,27	
TAP RT with warning stimulus	275,5	120	236,2	118	46,6	13	51,2	12	2,08	0,15	-0,39	-0,24 <sup>Δ</sup>
TAP RT working memory task	687,7	229	556,5	226	46,2	12	53,5	12	5,91	0,02*	-0,65	-0,36 <sup>Δ</sup>
TAP RT response shifting task	869,9	275	847,3	270	48,0	12	52,3	12	2,06	0,16	-0,38	
TAP RT divided attention task	702,5	96	665,8	94	42,8	10	46,8	10	2,56	0,12	-0,43	-0,69 <sup>Δ</sup>

<sup>1</sup> T-scores; lower value indicates poorer performance.  
<sup>2</sup> F-value for group effect adjusted for gender; \*: significant relative to original- $\alpha$ ; \*\*\*: significant relative to Bonferroni-adjusted  $\alpha$   
<sup>3</sup> Effect sizes (>0.2) relative to controls ( $d_1$ : adjusted for gender) and to the normative population ( $d_2$ );  $\Delta$ : potentially relevant effect.  
<sup>4</sup> Median effect sizes  
<sup>5</sup> T-value relative to controls

**Table 4. Neuropsychological results in 30 PCB-exposed and 30 control subjects.**

Figure 1

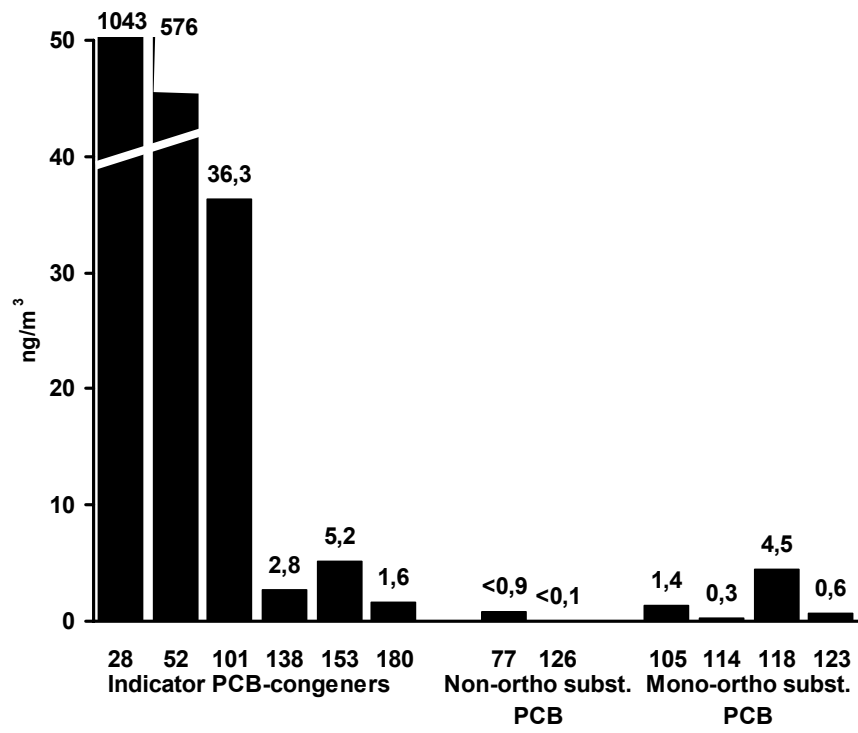


Figure 2

