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Postoperative cognitive dysfunction after cochlear implantation

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# 1 Postoperative cognitive dysfunction 2 after cochlear implantation

3 Annes J. Claes, MSc<sup>1,2\*</sup>, Suzanne de Backer, MD<sup>3</sup>, Paul Van de Heyning, MD PhD<sup>1,2</sup>,  
4 Annick Gilles, PhD<sup>1,2,4</sup>, Vincent Van Rompaey, MD PhD<sup>1,2</sup>, Griet Mertens, PhD<sup>1,2</sup>

5 <sup>1</sup>Department of Otorhinolaryngology, Head and Neck Surgery, Antwerp University Hospital,  
6 Antwerp, Belgium

7 <sup>2</sup>Experimental Laboratory of Translational Neurosciences and Dento-Otolaryngology, Faculty  
8 of Medicine and Health Sciences, University of Antwerp, Antwerp, Belgium

9 <sup>3</sup>Department of anesthesiology, Antwerp University Hospital, Antwerp, Belgium

10 <sup>4</sup>Department of Human and Social Welfare, University College Ghent, Ghent, Belgium

11

12 \* Corresponding author

13 Annes J. Claes

14 Wilrijkstraat 10

15 2650 Edegem (Belgium)

16 +32 3 821 58 38

17 annes.claes@uza.be

18 ORCID: 0000-0002-9447-5984

19

20 Suzanne de Backer

21 ORCID: /

22

23 Paul Van de Heyning

24 ORCID: 0000-0002-8424-3717

25

26 Annick Gilles

27 ORCID: 0000-0003-3669-6428

28

29 Vincent Van Rompaey

30 ORCID: 0000-0003-0912-7780

31

32 Griet Mertens

33 ORCID: 0000-0001-8621-0292

34

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38 Austria).

39

## 40 Abstract

41 Purpose: Postoperative cognitive dysfunction (PCD) is a subtle, prolonged  
42 deterioration in cognition after surgery. This complication has been frequently  
43 investigated, mainly after major (cardiac) surgery. However, the incidence after  
44 cochlear implantation is unknown. Therefore, the aim of the study was to investigate  
45 the incidence and possible risk factors of PCD in severely hearing-impaired older  
46 adults after cochlear implantation.

47 Methods: In a prospective cohort study, 26 older participants (age: M=70, SD=8 years),  
48 scheduled for cochlear implantation, were assessed prior to and one week after  
49 implantation by means of the Montreal Cognitive Assessment (MoCA). The incidence  
50 of PCD was calculated. In addition, the following possible risk factors were recorded:  
51 age, sex, education, duration of hearing impairment, preoperative signs of depression  
52 and anxiety, duration of anesthesia, anesthetic and surgical events and postoperative  
53 complications.

54 Results: The incidence of PCD was 11.5%, defined by a Z-score of change in MoCA  
55 scores  $\geq 1.96$  (i.e. a decrease of  $\geq 4$  points). The incidence of PCD was corrected for  
56 practice effects by incorporating data from a reference group. Besides an effect of age  
57 on the postoperative cognitive performance, no significant risk factors were identified.

58 Conclusions: The incidence of PCD after cochlear implantation is lower than after  
59 major surgeries, but higher than after other minor surgeries. Routine cognitive  
60 screening before and after cochlear implantation is recommended to identify patients  
61 with PCD and to provide additional care for these patients.

62

## 63 Key words

64 Postoperative cognitive dysfunction – cochlear implantation – Montreal Cognitive  
65 Assessment – postoperative cognitive decline – older adults – hearing impairment

66

67

## 68 Introduction

69 Due to the improvements of health and living standards during the past century, the  
70 world population has been growing and aging (Roser & Ortiz-Ospina, 2017). In 2015,  
71 twelve percent of the global population was aged 60 years or over and by 2050, this  
72 percentage of older adults is expected to more than double (United Nations-  
73 Department of Economics and Social Affairs-Population Division, 2015). Since overall  
74 life expectancy and the number of older adults is increasing, the number of older adults  
75 undergoing anesthesia is growing as well. By the age of 65, half of all people may have  
76 had one or more operations (Fodale, Santamaria, Schifilliti, & Mandal, 2010; Hazen,  
77 Larsen, & Martin, 1997). However, older adults are more vulnerable to adverse effects  
78 of surgery, anesthesia and perioperative care than younger adults due to the  
79 pathophysiological changes of aging (Chambers & Allan, 2017). In terms of  
80 neurological adverse effects, older adults demonstrate a higher incidence of  
81 postoperative cognitive dysfunction (PCD) (Strom, Rasmussen, & Sieber, 2014).

82

83 PCD refers to a subtle prolonged deterioration in cognition after surgery, with  
84 limitations in memory, intellectual ability and executive function, usually lasting for  
85 weeks or months (Chambers & Allan, 2017; Deiner & Silverstein, 2009; Strom et al.,  
86 2014). PCD is distinct from delirium, in that delirium either occurs during the transition  
87 from anesthesia to wakefulness and resolves within minutes or hours (emergence  
88 delirium) or develops as an acute brain syndrome within the first few postoperative  
89 days after an initial lucid period (postoperative delirium) (Strom & Rasmussen, 2014).  
90 Delirium is characterized by a fluctuating mental status, reduced awareness of the  
91 environment, disturbances in attention and hallucinations, and was previously known  
92 as psychosis (Deiner & Silverstein, 2009; Krenk & Rasmussen, 2011).

93

94 Although the exact pathophysiology of PCD remains to be elucidated, central  
95 neuroinflammation after surgery, cerebrovascular white matter disease and pre-  
96 existing Alzheimer's disease pathology may play a role (Berger et al., 2015). The  
97 diagnosis of PCD entails a comparison between pre- and postoperative  
98 neuropsychological testing. However, which tests are required to assess PCD and how  
99 much of a decline is required to define PCD is yet to be determined (Berger et al.,  
100 2015). The absence of formal diagnostic criteria for PCD is illustrated by the lack of a

101 PCD code in the 10<sup>th</sup> revision of the International Classification of Disease and Related  
102 Health Problems (ICD-10) (World Health Organization, 1992) and by the fact that PCD  
103 is not listed in the 5<sup>th</sup> edition of the Diagnostic and Statistical Manual of Mental  
104 Disorders (DSM-5) (American Psychiatric Association, 2013). Nonetheless, an  
105 important step towards consensus regarding the diagnostic criteria of PCD was made  
106 by the International Study of Postoperative Cognitive Dysfunction (ISPOCD) research  
107 group, which set diagnostic guidelines (Rasmussen et al., 2001) and applied it in a  
108 large number of multi-centric studies (e.g. Canet et al., 2003; Johnson et al., 2002;  
109 Moller et al., 1998; Rasmussen et al., 2003; Steinmetz et al., 2009). Some key  
110 elements of these guidelines are the use of objective neuropsychological tests (no  
111 questionnaires), preferably with equivalent alternate forms, good sensitivity and  
112 without floor and ceiling effects. The evaluation must be performed *before* surgery,  
113 most optimally one to two weeks preoperatively, and *after* surgery, for instance one  
114 week and three months postoperatively (Johnson et al., 2002; Moller et al., 1998). Also  
115 data from a control group using the same test battery and the same intervals should  
116 be available and should be incorporated in a Z-score calculation in order to correct for  
117 practice effects. A Z-score larger than 1.96 corresponds to a severe and unexpected  
118 deterioration in cognition, as only 2.5% of the controls presents such a large Z-score.

119  
120 By means of these diagnostic criteria, an association has been established between  
121 PCD and decreasing activities of daily living (Moller et al., 1998). Moreover, PCD also  
122 has long-term effects: PCD after non-cardiac surgery has been related to increased  
123 mortality, risk of leaving the labor market prematurely, and dependency on social  
124 transfer payment over a period of eight years (Steinmetz et al., 2009). The incidence  
125 of PCD was found to be higher after cardiac and certain types of orthopedic surgery  
126 (i.e. hip replacement) than after non-cardiac surgery (Sauer, Kalkman, & van Dijk,  
127 2009; Steinmetz & Rasmussen, 2016; van Harten, Scheeren, & Absalom, 2012).  
128 Incidence is also higher after major surgical procedures compared to minor  
129 procedures, defined by an anticipated hospital stay of only one night, and in case of  
130 complications (Sauer et al., 2009; Strom & Rasmussen, 2014). Irrespective of the type  
131 of surgery, the predominant risk factor for PCD is advanced age. Johnson et al. (2002)  
132 investigated the incidence of PCD after major non-cardiac surgery in middle-aged  
133 adults between 40 and 60 years old and found an incidence of 19%, compared to 26%  
134 in adults older than 60 years (Moller et al., 1998), both using the same,

135 abovementioned criteria for PCD. Additionally, the patient's medical conditions play a  
136 role in the pathogenesis of PCD: possible patient-related risk factors are hypertension,  
137 modifications in thyroid hormone functioning, history of cerebrovascular accident,  
138 history of substance abuse, preoperative cognitive impairment, etc. Lower educational  
139 level is another major predisposing factor for PCD (Fodale et al., 2010; Strom et al.,  
140 2014).

141  
142 Whereas PCD after cardiac and non-cardiac major surgery has been fairly well  
143 documented, the incidence of PCD after minor surgery has only been investigated by  
144 few researchers. For instance, the ISPOCD2 investigators demonstrated an incidence  
145 of PCD of nearly 7% in 372 older patients 7 days after minor surgery under general  
146 anesthesia (Canet et al., 2003). Moreover, on the first day after minor surgery a PCD  
147 incidence of as much as 47% in 30 older adults was reported by Rohan et al. (2005),  
148 using the ISPOCD criteria. The incidence was the same for both intravenous (propofol)  
149 and inhaled anesthesia (sevoflurane). Cochlear implantation is also considered a  
150 minor, routine surgical procedure for the management of severe to profound  
151 sensorineural hearing loss. In most cases, surgery is performed under general  
152 anesthesia and requires an anticipated hospital stay up to one night. Two to four weeks  
153 after the implantation, the external part, i.e. the speech processor, is activated and  
154 from then onwards, sounds are transmitted electrically to the hearing nerve. Cochlear  
155 implantation has been reported to be a safe and efficient hearing solution, even in older  
156 adults, with no major and only few minor surgical complications (Benatti, Montino,  
157 Girasoli, Trevisi, & Bovo, 2013; Coelho, Yeh, Kim, & Lalwani, 2009; Lundin, Nasvall,  
158 Kobler, Linde, & Rask-Andersen, 2013). Therefore, it was concluded that cochlear  
159 implantation should not be denied to older adults with severe to profound hearing loss  
160 who are otherwise in good health (Cosetti & Lalwani, 2015). However, earlier research  
161 has not investigated PCD as a possible complication of cochlear implantation, leaving  
162 the incidence of PCD after this type of surgery unknown.

163  
164 Therefore, the present study aims to investigate the incidence of PCD in older, severely  
165 to profoundly hearing-impaired older adults at one week after cochlear implantation.  
166 Furthermore, the effect of several possible risk factors on the incidence of PCD is  
167 explored, namely age, sex, years of education, occurrence of surgical and anesthetic  
168 events and complications, and duration of anesthesia, as these have been put forward

169 as risk factors in previous research. Additionally, the possible effect of duration of  
170 hearing loss and preoperative states of anxiety and depression are examined. These  
171 factors are specifically of interest in a severely hearing-impaired population, since  
172 hearing deprivation may affect general mental health and mood and, in turn, cognitive  
173 performance.

174

## 175 Material and methods

### 176 Participants

177 CI candidates who met the following inclusion criteria were enrolled in the study: Every  
178 participant (1) was Dutch-speaking, (2) was at least 55 years old, (3) was scheduled  
179 for unilateral cochlear implantation in the Antwerp University Hospital, (4) had bilateral  
180 severe to profound hearing loss (mean threshold at 0.5, 1 and 2 kHz  $\geq$  85 dB HL in the  
181 better-hearing ear), fulfilling the national criteria for reimbursement of cochlear  
182 implantation in Belgium and (5) had a postlingual onset of the hearing impairment.  
183 Participants were excluded in the case of serious uncorrected vision impairments  
184 which would impede the bimodal administration of the cognitive assessment and if the  
185 implantation involved a re-implantation or a contralateral implantation. Preoperatively  
186 present cognitive impairment was *not* a reason for exclusion from the study. Twenty-  
187 six consecutive participants (16 males, 10 females) were invited to participate in the  
188 study, and all of them agreed. The median age was 70.5 years, ranging from 55 to 83  
189 years. Participants had between 8 and 16 years of formal education, starting to count  
190 from the age of 6 (median: 12 years). The median duration of severe hearing loss was  
191 21 years, ranging from 0.3 to 50 years. Prior to implantation, 8 participants used  
192 hearing aids bilaterally (30.8%), 12 unilaterally (7 right, 5 left) (46.2%) and 6 did not  
193 use hearing aids (23.1%). Of the 12 preoperatively unilaterally aided participants, 7  
194 were implanted in their better, i.e. aided, ear and five were implanted in their worse,  
195 i.e. non-aided, ear. Participants' demographics are given in Table 1.

196



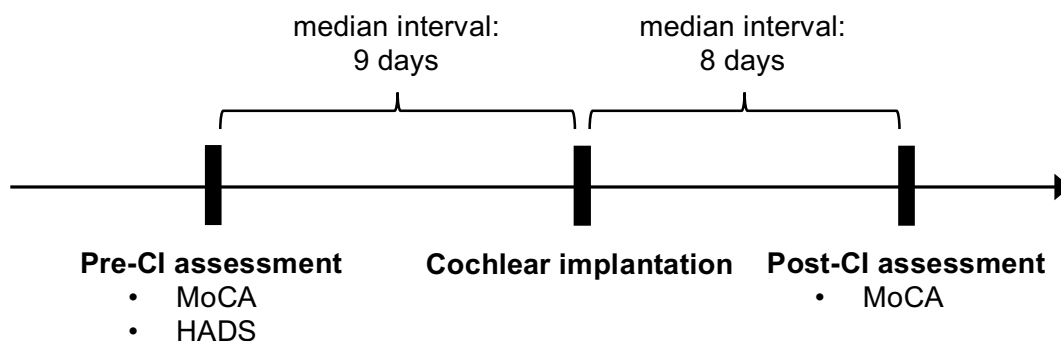
197 **Table 1. Demographics and results of the participants (n=26).** Formal education is the number of years of education starting from the age of 6. CI: cochlear implantation, f:  
 198 female, HADS: Hospital Anxiety and Depression Scale, HL: hearing loss, m: male, MoCA: Montreal Cognitive Assessment, Preop: preoperatively.

	Sex	Age (year)	Duration of HL (year)	Formal education (year)	HA use preop.	Side of implantation	Better or worse ear implanted?	Pre-CI HADS score: Depression	Pre-CI HADS score: Anxiety	Duration of anesthesia	Post-CI hospital stay (days)	Pre-CI MoCA score	Post-CI MoCA score	Change in MoCA score (post – pre)
1	f	70	20	13	No	Left	Undefined	10	6	3:08	1	24	24	0
2	m	76	50	8	Bilateral	Right	Undefined	5	12	3:24	1	21	25	4
3	f	69	30	10	Right	Right	Better	11	12	4:26	1	12	15	3
4	m	83	40	9	No	Left	Undefined	14	7	3:42	2	18	18	0
5	m	76	45	12	Left	Left	Better	9	6	3:09	1	19	19	0
6	m	70	10	10	Right	Left	Worse	0	1	3:59	1	26	29	3
7	f	65	35	9	No	Right	Undefined			4:06	2	26	25	-1
8	m	57	10	14	No	Left	Undefined	8	3	3:19	1	25	22	-3
9	m	77	16	10	Right	Right	Better	5	8	4:22	1	22	20	-2
10	f	80	18	8	Right	Left	Worse	10	3	4:19	1	23	23	0
11	m	63	45	10	Right	Right	Better	9	9	3:35	1	21	24	3
12	m	62	4	8	Left	Left	Better	9	8	3:02	1	19	22	3
13	m	67	20	8	Left	Left	Better	5	3	3:10	1	19	22	3
14	m	76	0.3	13	No	Right	Undefined	4	7	3:18	1	24	20	-4
15	m	56	26	10	Bilateral	Right	Undefined	6	4	3:15	1	24	25	1
16	m	66	36	14	Bilateral	Right	Undefined	13	3	3:50	1	24	26	2
17	f	74	20	15	Bilateral	Right	Undefined	8	9	3:28	1	25	25	0
18	m	81	27	8	Bilateral	Right	Undefined	10	5	3:39	1	24	23	-1
19	m	71	14	16	Left	Left	Better	15	13	2:59	1	21	24	3
20	f	77	4	12	No	Right	Undefined	5	4	3:23	1	11	7	-4
21	f	56	11	14	Bilateral	Left	Undefined	10	15	3:04	1	29	27	-2
22	m	72	3	15	Right	Left	Worse	5	5	4:37	1	25	29	4
23	m	55	8	16	Right	Left	Worse	5	4	3:27	1	25	21	-4
24	f	67	28	12	Bilateral	Right	Undefined	2	3	2:45	1	25	26	1
25	f	72	15	12	Left	Right	Worse	5	10	3:09	1	23	24	1
26	f	77	15	12	Bilateral	Right	Undefined	6	2	2:05	1	24	25	1

199  
200

## Study design

In this observational, prospective study, participants were assessed twice, shortly before and at one week after cochlear implantation. Assessments were planned at the day of the preoperative appointment (typically one to two weeks prior to surgery) and the one-week postoperative appointment with the surgeon, in accordance with the guidelines of Rasmussen et al. (2001). During the preoperative assessment a cognitive test, the Montreal Cognitive Assessment (MoCA) (Nasreddine et al., 2005), was performed and one questionnaire, the Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith, 1983), was administered to evaluate states of anxiety and depression shortly before implantation. During the postoperative assessment the MoCA was repeated. The preoperative assessment was performed at a median of 9 days (range: 0 to 70 days) before surgery and the second at a median of 8 days after surgery (range: 5 to 20 days after implantation). In each participant, the postoperative assessment was performed prior to the activation of the speech processor, meaning that the participant could not yet hear through the cochlear implant. The median number of days between both measurements was 19 days (range: 10 to 87 days). For one participant the implantation was postponed, resulting in a longer interval between both measurements. An overview of the study design is provided in Fig 1.



**Fig 1 Schematic overview of the prospective study design**

CI: Cochlear implantation, HADS: Hospital Anxiety and Depression Scale, MoCA: Montreal Cognitive Assessment.

## Ethics

This study was conducted in accordance with the recommendations of the ethics committee of the Antwerp University Hospital/University of Antwerp. The protocol was approved on June 15th, 2015 (protocol number 15/17/181). All participants gave

written informed consent in accordance with the Declaration of Helsinki prior to participation.

### Cognitive assessment

The Montreal Cognitive Assessment (MoCA) (Nasreddine et al., 2005) was used to assess cognition in the present study. The MoCA is a one-page 30-point screening tool to identify mild cognitive impairment. It is administered in 10 to 15 minutes and assesses short-term memory, visuospatial abilities, executive functions, phonemic fluency, verbal abstraction, attention, concentration, working memory, language and orientation to time and place. Higher scores indicate better cognition. Consistent with Nasreddine et al. (2005), a correction for education effects was applied by adding one point to the total score for participants with 12 years of formal education or less. The cognitive assessment was carried out in a quiet room and only the participant and the investigator were present. Visual support by means of a time-fixed PowerPoint presentation was added in order to prevent the participants' hearing loss from negatively affecting the cognitive performance (Dupuis et al., 2015). The PowerPoint presentation was presented on an external screen in front of the participant and displayed the written instructions for each task. In addition, the written equivalent of the items for the Memory task, the Attention task (Forward and Backward Digit Span and Vigilance) and the Sentence Repetition task was presented, providing simultaneous, bimodal (both visual and oral) stimulation to the participant. Where needed, the slides were time-fixed in accordance to the administration guidelines. Since the MoCA has been demonstrated to be susceptible to practice effects, particularly between the first and second administrations (Cooley et al., 2015), version A and alternate version B were used in the present study.

### Hospital Anxiety and Depression Scale (HADS)

In order to identify depression and anxiety prior to implantation, the HADS was administered. This is a reliable instrument for detecting states of depression and anxiety (Zigmond & Snaith, 1983). This self-assessment questionnaire consists of seven items in the subscale Depression (e.g.: "I still enjoy the things I used to enjoy.") and seven items in the subscale Anxiety (e.g.: "I get a sort of frightened feeling as if something awful is about to happen.").

## Cochlear implantation

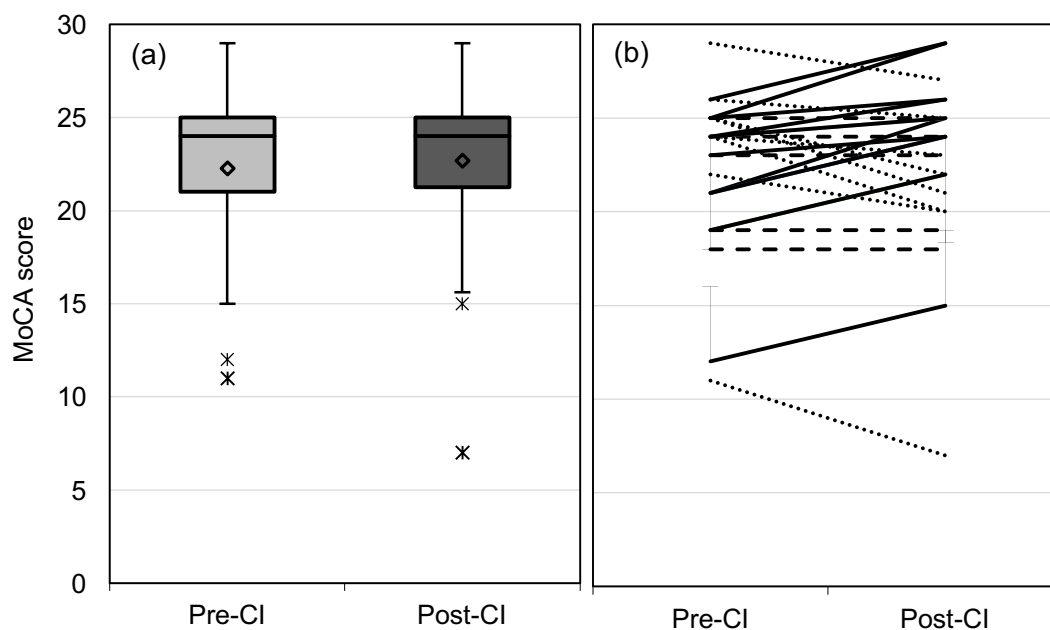
In all study subjects, structure preservation surgery was intended (Kiefer et al., 2004). All patients underwent general anesthesia with intravenous infusion of propofol and remifentanyl and the duration of anesthesia was recorded. There was standard monitoring of blood pressure, pulse oxymetry, continuous electrocardiogram (ECG) monitoring and monitoring of ventilation and end tidal carbon dioxide (etCO<sub>2</sub>). Prior to the skin incision, 1 g amoxicillin/clavulanic acid and 80 mg methylprednisolone were administered. Postoperatively, oral methylprednisolone therapy was continued for 14 days in a daily decreasing dosage. Peri- and postoperative events and complications were recorded, for instance perioperative hypotension (defined as a deviation of 10% from the preoperative value) and facial nerve paralysis, pain, fever, vertigo, etc. after surgery.

## Statistical methods

OpenClinica LLC (Waltham, USA) was used for data storage. This is a password protected online database for electronic data capture and data management developed for clinical research. The presence of PCD is defined by a Z-score of the change in MoCA scores of 1.96 or more (a positive Z-score corresponds to a deterioration in MoCA scores), as described in the guidelines by Rasmussen et al. (2001). According to this method, the Z-scores are calculated by subtracting the average learning effect (i.e. mean change in MoCA scores of a reference group) from the individual changes, and dividing the result by the standard deviation for the MoCA score changes of the reference group. Data from the test-retest reliability study by Nasreddine et al. (2005) are used as reference in the present study, since the characteristics of the study design and the participants were similar: Nasreddine et al. (2005) performed the MoCA in 26 participants, on average, 35 days (SD=17.6 days) apart, compared to 26 participants examined, on average, 24 days (SD=19.6 days) apart in the present study. Statistical analyses were performed using IBM SPSS Statistics version 24 (IBM Corp., New York, NY). General linear models with either MoCA Post-CI scores or change in MoCA scores as the independent variable, and possible risk factors as covariates or fixed factors were run to explore associations. Statistical significance was defined as  $p < 0.05$ .

## Results

Preoperatively, the mean MoCA score was 22.3 points (SD=4.1). The highest score was 29 and the lowest 11. Postoperatively, the mean MoCA score was 22.7 points (SD=4.5), ranging from 7 to 29 (Fig 2a). Five participants (19%) had the same MoCA score on both measurements. Eight of the participants (31%) showed a decrease in MoCA score at the Post-CI measurement, whereas thirteen participants (50%) showed an increase in MoCA score (Fig 2b). The increase in MoCA scores is presumably due to practice effects and natural variation. The mean change in MoCA scores was 0.4 points (SD=2.5) and the maximal change was -4 and +4 points. The MoCA Pre-CI scores were strongly correlated to the MoCA Post-CI scores ( $r=0.84$ ,  $p<0.001$ ). These data are similar to the MoCA test-retest reliability data, collected from 26 participants and reported in Nasreddine et al. (2005): the mean change was 0.9 points (SD=2.5 points), compared to 0.4 points (SD=2.5) in the present study, and the correlation between the two evaluations was  $r=0.92$  ( $p<0.001$ ), compared to  $r=0.84$  ( $p<0.001$ ) found in the current study. Participants' individual results are given in Table 1.



**Fig 2 Distribution of the MoCA scores (a) and the individual change in MoCA scores (b) prior to implantation (Pre-CI) and after implantation (Post-CI)**

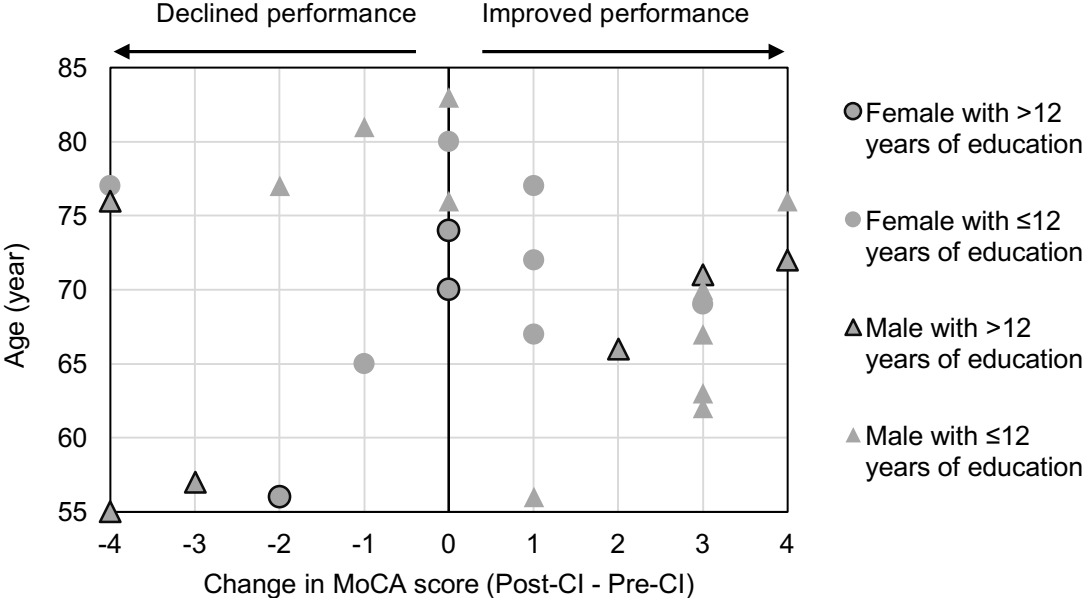
(a) The box of the box-and-whiskers plot represent the 1st quartile, median and 3rd quartile. The mean score is indicated by the diamond. The whiskers connect the minimal and maximal score within  $1.5 \times$  interquartile distance from the 1<sup>st</sup> and the 3<sup>rd</sup> quartile. Scores outside this range (outliers) are indicated by asterisks. (b) Solid lines indicate

an increase in MoCA score, dashed lines represent stable scores and dotted lines indicate decreased MoCA scores. CI: Cochlear implantation, MoCA: Montreal Cognitive Assessment.

Incidence of PCD was 11.5% (3 out of 26 participants). These three participants (ID number 14, 20 and 24 in Table 1) demonstrated a decrease of 4 points postoperatively. They had an initial MoCA score of 24, 11 and 25 respectively, indicating that a clinically significant decline was both present in good and poor performers. There were no unusual events or complications in the patients with PCD. In each of these three participants, the duration of anesthesia was lower than the overall average: respectively 3h 18min., 3h 12min. and 3h 27min., compared to the overall mean of 3h 29min (SD=34 min.). In one of these three participants, no anesthetic or surgical complications occurred. In one of them, brief periods of hypotension were observed during anesthesia, but no postoperative complications, and in the third patient, the anesthesia was uneventful, but the patient reported some pain at the surgical site when blowing his nose. In the general group of 26 CI recipients, brief periods of hypotension occurred in 23% and postoperative pain at the surgical site was reported by 19% of participants. For the three patients with PCD the hospital stay was one night, as anticipated. None of these participants was implanted in the better ear. They were either implanted in the worse ear, i.e. the ear without hearing aid, or in one of similar performing ears, in the case of bilateral hearing aid use or no hearing aid use. Moreover, not all participants who performed very poorly prior to surgery presented a decrease postoperatively, as is shown by the participant with an initial MoCA score of 12 and a subsequent MoCA score of 15 (Fig 2b).

A general linear model with MoCA Post-CI scores as dependent variable and MoCA Pre-CI scores and Age as covariates, indicated that both covariates had a significant effect on the MoCA Post-CI results, independently of each other's effect and independently of the interaction effect (MoCA Pre-CI score:  $p=0.029$  and Age:  $p=0.005$ ). Higher MoCA Pre-CI scores were associated with higher Post-CI scores, and higher age with lower Post-CI scores. None of the other possible risk factors appeared to be significant (duration of anesthesia, education, HADS results, sex or duration of hearing loss). A second general linear model included the change in MoCA scores as dependent variable. Only the MoCA Post-CI scores were significantly associated to the change in MoCA scores ( $p=0.022$ ). The other factors, namely

duration of anesthesia, MoCA Pre-CI score, education, age (Fig 3), HADS results, sex or duration of hearing loss did not present a significant effect.



**Fig 3 Change in MoCA score across both measurements (MoCA Post-CI minus MoCA Pre-CI) in relation to age**

Improvements result in positive differences and declines result in negative difference. CI: Cochlear implantation, MoCA: Montreal Cognitive Assessment.

## Discussion

The aim of the study was to determine the incidence of PCD at one week after cochlear implantation under general anesthesia. This kind of surgery is categorized as minor because of the expected postoperative stay of up to one night. Currently, no formal diagnostic criteria for PCD are available and many different methodologies have been used to determine how much dysfunction or decline is clinically significant (Deiner & Silverstein, 2009). However, extensive research by the ISPOCD group has increased the conformity regarding the diagnosis of PCD and their guidelines (Rasmussen et al., 2001) have been adopted as well as possible in the present study. The incidence of PCD was found to be 11.5% after cochlear implantation, determined by a Z-score of the change of 1.96 or more compared to a reference group (equal to a deterioration  $\geq$  four points on the MoCA, in the present study). These results highlight that a considerable number of patients suffers from PCD, even after relatively minor surgery. The participants who developed PCD did not appear to be deviating from the overall group in terms of number of surgical or anesthetic events and complications, duration of anesthesia, duration of hospital stay or side of implantation (better or worse ear). Concerning the latter factor, all three participants with PCD had been implanted either in the worse ear, i.e. the ear without a hearing aid, or in one of similar performing ears, in the case of bilateral hearing aid use or no hearing aid use. In other words, in these participants the hearing capabilities had not drastically been decreased after implantation. Therefore, based on these limited data, it seems unlikely that the side of implantation impacts upon the incidence of PCD.

The definition of PCD, based on Z-scores was also adopted by Rohan et al. (2005) and Canet et al. (2003), who investigated the incidence of PCD respectively on the first day, and seven days and three months after minor surgery. On the first day after minor surgery an incidence of 47% was observed (Rohan et al., 2005), whereas the incidence at one week and three months postoperatively was 6.8% and 6.6% (Canet et al., 2003). Compared to the one week postoperative results of Canet et al. (2003), the incidence of PCD is found to be somewhat higher in the present study (6.8% vs 11.5%). Several differences between both studies may explain the distinction in incidence. First of all, surgery and anesthesia types may impact on cognition to a different extent. Cochlear implantation requires a hospital stay of at least one night,



whereas the surgical procedures in the study of Canet et al. (2003) could either be performed on an in- or an out-patient care basis according to local practice at each participating hospital. This may imply that cochlear implantation is slightly more burdensome than the surgeries in Canet et al. (2003), possibly impacting cognition to a greater extent. In addition, Canet et al. (2003) excluded participants with dementia as defined by a Mini-Mental State Examination score lower than 24, in contrast to the present study, in which no exclusion criteria were applied with regard to preoperative cognition. As preoperative cognitive impairment has previously been related to postoperative cognitive dysfunction (however, this is not demonstrated in the current study), not excluding participants with poor preoperative cognition in this study may have led to a higher incidence compared to Canet et al. (2003). Out of the three participants who showed a decline in performance of four points in the current study, one participant indeed had a poor preoperative performance of 11 points on the MoCA.

How the incidence of PCD evolves in the long term, for instance at three or six months after cochlear implantation, was not investigated in the present study. The reason for this is the possible positive effect of cochlear implantation on cognition in hearing-impaired older adults, after the external part (i.e. the speech processor) has been activated to transmit auditory signals to the auditory nerve. The speech processor is usually activated two to four weeks after surgery, once the surgical wound has healed sufficiently. Indeed, some studies suggest that a cochlear implant improves cognition as early as six and twelve months after the implantation (Cosetti et al., 2016; Mosnier et al., 2015). In order to avoid the impact of using the speech processor, it was decided to only investigate the incidence of PCD shortly after implantation and prior to the activation of the speech processor, namely at one week after implantation. In our opinion, it is ethically unreasonable to determine the pure incidence of PCD after cochlear implantation at a longer interval than several weeks, as this would imply that the activation of the speech processor has to be significantly postponed and the participant remains severely hearing-impaired for a longer period than needed.

The secondary goal of the study was to investigate the association between possible risk factors of PCD and cognitive performance after cochlear implantation. Prior studies found advanced age as the predominant risk factor for PCD (Deiner & Silverstein, 2009; Fodale et al., 2010; Sauer et al., 2009). Indeed, age significantly accounted for

variability in postoperative cognition, beyond the effect of preoperative cognitive functioning. However, it did not impact upon the amount of *change* in cognitive performance. As PCD is defined by a significant *decline* in cognitive functioning, rather than by a certain *cut-off* in postoperative functioning, the findings of the present study do not completely confirm the effect of age on PCD. Other possible risk factors of PCD, namely duration of anesthesia, years of formal education, duration of hearing loss, preoperative depression and anxiety, and sex, were also investigated, but no significant effect on postoperative cognition, neither on the change in cognition, was demonstrated. Larger sample sizes are needed to further investigate the effect of these factors on the occurrence of PCD after cochlear implantation. On the other hand, peri- and postoperative administration of methylprednisolone may have been a protective factor against PCD in the present study, as it suppresses the immune system and decreases inflammation. This is supported by a study of Qiao et al. (2015), in which treatment with methylprednisolone was associated with a lower incidence of PCD in elderly patients undergoing major surgery. However, it may as well have a negative effect on the occurrence of PCD by deregulating glucose levels (Tamez Perez et al., 2012).

In the present study, cognition was assessed by means of the MoCA. Although this is a short cognitive screening tool, the MoCA scores did not present ceiling or floor effects and were roughly normally distributed prior to and after surgery. This suggests that the MoCA was not too easy neither too difficult for the study population. A major advantage of the MoCA over other screening tests is the breadth of cognitive domain coverage: besides short-term memory, also visuospatial abilities, executive functions, phonemic fluency, verbal abstraction, attention, concentration, working memory, language and orientation to time and place are assessed (Appels & Scherder, 2010; Vogel, Banks, Cummings, & Miller, 2015). Furthermore, because of the short administration time, the negative effect of fatigue is kept to the minimum. The MoCA is also easy to administer and provides alternate versions, which have been proven to be equivalent (Costa et al., 2012; Costa et al., 2014; Wu, Dagg, & Molgat, 2017). Since the patients of the current study were all to undergo cochlear implantation, they all suffered from severe to profound hearing loss. Considering the negative effect of sensory impairment on the performance of cognitive tests (Dupuis et al., 2015) and the specific characteristics of the study population, a cognitive test modified for hearing-impaired individuals was

necessary. As no cognitive assessment tool for the hearing-impaired was available at the start of the present study, it was decided to adapt the MoCA by providing bimodal stimulation (both visual and oral). However, very recently the Hearing-Impaired MoCA (HI-MoCA) has been developed and validated in cognitively intact adults over the age of 60 (Lin et al., 2017). The HI-MoCA is a version of the MoCA specifically for the hearing-impaired without any verbal cues. Future research should consider the HI-MoCA as a reliable tool for screening cognitive impairment in severely hearing-impaired individuals.

Even though the present study has some limitations, such as the small sample size and the lack of long-term assessments (due to ethical limitations, as discussed above), it also has several strengths. First of all, there were no missing data. Missing data, especially if they are due to unwillingness to participate, are difficult to handle, because the reason for unwillingness may be a cognitive problem. Therefore, excluding these participants runs the risk of underestimating the PCD incidence (Rasmussen et al., 2001). Another strength of the study is the wide variety in preoperative cognitive function by not excluding participants if they performed lower than a given cut-off. This leads to a representative sample of older adults undergoing unilateral cochlear implantation under general anesthesia.

## Conclusion

Given the considerably high incidence of PCD of 11.5% at one week after cochlear implantation, a routine cognitive screening before and after surgery in older adults is recommended. In some hospitals, a cognitive screening is already part of the CI candidacy evaluation, but a second evaluation should be implemented postoperatively to evaluate the occurrence of PCD. Tailored postoperative care and assistance must be provided for patients who present a relevant decline in postoperative cognitive performance and presence PCD should be considered in deciding whether the patient can be discharged. As minor surgeries are being performed more often on an out-patient basis or with a strictly minimal duration of hospitalization, a pre- and postoperative cognitive screening becomes more important. Indeed, the presence of PCD may go unnoticed without appropriate screening, both for the clinician and the patient. Once the patient is discharged from the hospital, the consequences of PCD

for the patient may, however, be more pronounced, whereas care and treatment are less readily available at home.

## Conflict of interest

No conflicts of interest were declared by the authors.

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