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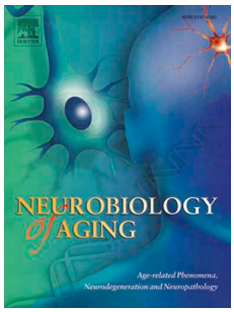

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Visual and visuomotor interhemispheric transfer time in older adults

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Abstract

Older adults typically experience reductions in the structural integrity of the anterior channels of the corpus callosum (CC). Despite preserved structural integrity in central and posterior channels, many studies have reported that interhemispheric transfer, a function attributed to these regions, is detrimentally affected by aging. In this study, we use a constrained ERP analysis in the theta and alpha frequency bands to determine whether interhemispheric transfer is affected in older adults. The crossed-uncrossed difference (CUD) and lateralized visual evoked potentials were used to assess interhemispheric transfer in young (18-27) and older adults (63-80). We observed no differences in the CUD measure between young and older groups. Older adults appeared to have elongated transfer in the theta band potentials, but this effect was driven by shortened contralateral peak latencies, rather than delayed ipsilateral latencies. In the alpha band, there was a trend towards quicker transfer in older adults. We conclude that older adults do not experience elongated interhemispheric transfer in the visuomotor or visual domains, and that these functions are likely attributed to posterior sections of the CC, which are unaffected by aging.

Keywords: interhemispheric transfer, interhemispheric transmission, aging, Poffenberger, corpus callosum

1. Introduction

Aging is associated with white matter degeneration in the brain (Barrick, Charlton, Clark, & Markus, 2010; Bastin et al., 2010; Davis et al., 2009; Tang, Nyengaard, Pakkenberg, & Gundersen, 1997). In particular, damage to the structure known as the corpus callosum (CC) is a strong predictor of global cognitive and motor deterioration in later life (Frederiksen et al., 2012; Jokinen et al., 2007; Penke et al., 2010; Ryberg et al., 2011). The evidence from neuroimaging suggests that differential patterns of degeneration in the CC may be related to typical and pathological aging (Bastin et al., 2010; Penke et al., 2010; Salat et al., 2005). For example, white matter integrity in the posterior section of the CC has been related to processing speed, hypertension and cognitive abilities in older adults (Penke et al., 2010; Wong, Ma, & Lee, 2017a). Therefore, rigorous measurement of the CC and its associated functions has the potential to provide important information about how the brain ages successfully and unsuccessfully.

Neuroimaging has provided valuable insight into how the structure of the CC is affected by aging (Frederiksen et al., 2012; Sullivan, Rohlfing, & Pfefferbaum, 2010). It has increasingly been shown that white matter integrity in the aging CC follows an anterior-posterior gradient of decline. Age-related degeneration of CC fibres occur primarily in the anterior section known as the genu (Bastin et al., 2008, 2010; Hou et al., 2012; Madden et al., 2009; Salat et al., 2005), which consists of small-diameter fibres that connect the frontal lobes. In contrast, the more posterior splenium, which connects the occipital lobes, appears to be spared in older adults (Bastin et al., 2010; Hou et al., 2012; Salat et al., 2005). While these specific patterns have been well documented and replicated, less emphasis has been placed on the assessment of functions that may be targeted by age-induced alterations to specific CC subsections. A primary function of the CC is to facilitate information transfer between hemispheres (Bloom & Hynd, 2005; Brown, Bjerke, & Galbraith, 1998; Rugg, Milner, & Lines, 1985), a process

known as interhemispheric transfer. For example, a stimulus observed through the left visual hemifield, and therefore processed by the contralateral right hemisphere, needs to be transferred to the left hemisphere before making a right hand response to that stimulus. This process was exploited in a classic paradigm pioneered by Poffenberger (1912), which attempts to measure interhemispheric transfer time (IHTT). The paradigm considers the difference in reaction times (RTs) through the interhemispheric (crossed; e.g. left hemifield - right hand) and intrahemispheric (uncrossed; e.g. left hemifield - left hand) response pathways, known as the crossed-uncrossed difference (CUD). IHTT can also be measured via the lag between ipsilateral and contralateral event-related potentials (ERP) that are evoked in response to the Poffenberger stimulus (Saron & Davidson, 1989b). Surgical sectioning or under-development of the CC is associated with slower IHTT (Brown et al., 1998; van der Knaap & van der Ham, 2011), suggesting that white matter degeneration in aging may also increase estimates of IHTT.

Despite the preservation of the splenium fibres, a number of studies have reported that IHTT is lengthened in older adults. This has been widely described by studies employing the CUD measure (Bellis & Wilber, 2001; Davis, Kragel, Madden, & Cabeza, 2012; Jeeves & Moes, 1996; Reuter-Lorenz & Stanczak, 2000), though others have failed to observe any aging effects (Linnet & Roser, 2012; Schulte et al., 2013). For the ERP measure, Curran et al. (2001) reported an increase in the latency of the ipsilateral P1 component in older adults, indicating an increase in IHTT. Hoptman et al., (1996) contrarily reported no difference in the latency of ipsilateral components between young and older groups, although there was a trend towards an elongated IHTT for older adults.

Inconsistent age effects and lack of correlations between the CUD and ERP (Saron et al., 1989) could be explained by the idea that behavioral and ERP measures describe IHTT through independent callosal pathways. Much evidence suggests that the CUD may rely on

transfer through more anterior CC regions, such as the CC midbody or even genu, rather than splenial fibres. Tomaiuolo, Nocentini, Grammaldo, & Caltagirone (2001) reported that the CUD (measured across > 2000 trials) was elongated in a patient with anterior lesions to the CC, while the splenium and rostrum were still intact. Similarly, Di Stefano, Sauerwein, & Lassonde (1992) found an increased CUD in two acallosal patients and one patient with anterior CC lesions. In contrast, Tassinari et al. (1994) did not observe an elongated IHTT in six patients with exclusively anterior or posterior regions. However, as evident in their report, midbody fibres were preserved in at least four of these patients, which may have protected their CUD estimates (Zaidel & Iacoboni, 2003). In healthy participants, Schulte et al (2005) observed that the CUD was significantly correlated with the genu and marginally with the splenium in healthy adults, indicating that the genu may be the more involved region. Furthermore, investigations of the Poffenberger paradigm using fMRI have yielded premotor, sensorimotor and prefrontal activations (Iacoboni & Zaidel, 2004; Tettamanti et al., 2002), as well as activations in the CC genu (Gawryluk, D'Arcy, Mazerolle, Brewer, & Beyea, 2010a; Omura et al., 2004; Tettamanti et al., 2002; Weber et al., 2005) and the CC midbody (Gawryluk, D'Arcy, Mazerolle, Brewer, & Beyea, 2010b), supporting a lack of involvement of posterior regions. Iacoboni & Zaidel (2004) found a strong correlation (r = 0.9) between the CUD and BOLD activity in the right superior parietal cortex, indicating that transfer as measured by the CUD may depend on CC midbody fibres that connect sensorimotor areas, rather than on the genu or splenium.

The possible dependence of the CUD on anterior interhemispheric pathways, coupled with age-related decline in the CC genu, may account for the reports of an increased CUD in older adults. However, these findings are less able to explain the reports of older age IHTT as measured by visual ERPs (Curran et al., 2001). Westerhausen et al. (2006) demonstrated that IHTT between contralateral and ipsilateral P1 peaks was correlated with posterior CC

integrity, indicating that the splenium fibres are the most likely pathway for visual transfer. Further investigations are clearly necessary to untangle which specific functions of the CC are affected by older age. In this paper we review the traditional measures of IHTT and propose a constrained ERP approach in order to revisit the issue of how IHTT is affected by aging.

Despite being widely used, the CUD and ERP measures are associated with various shortcomings. CUD estimates can be as low as 2ms (Iacoboni & Zaidel, 2000; Marzi, Bisiacchi, & Nicoletti, 1991), which is quicker than the conduction velocity of the largest callosal fibres (Aboitiz, Scheibel, Fisher, & Zaidel, 1992). Furthermore, the CUD often takes a negative value (e.g. Braun, Villeneuve, & Achim, 1996; Marzi et al., 1991; Tettamanti et al., 2002), unintuitively suggesting that there is no temporal cost associated with interhemispheric transfer. To date, nobody has been able to fully account for the negative CUD (Chaumillon, Blouin, & Guillaume, 2014; Derakhshan, 2006). Similarly, ERP estimates of IHTT can be negative. For instance, Saron et al. (2003) reported that peak latency measures of IHTT were in the anatomically predicted direction in only 80% of participants. The ERP approach requires the selection of peak latencies at the single-subject average level, which involves defining a time window around the component of interest and selecting the latency of the most prominent positive or negative peak. Single-subject averages do not always have an clear morphology (see e.g. Li, Bin, Hong, & Gao, 2010), likely due to trial-by-trial variability in the P1/N1 latencies. Ambiguity in peaks may lead to skewed estimates of the component latencies, thus conflating the estimate of IHTT.

Recent studies have demonstrated that visual evoked potentials like the P1 and N1 arise from event-related phase synchronisation of ongoing EEG oscillations in the theta (4-8 Hz) and alpha (9-14 Hz) frequency bands (Freunberger et al., 2008; Gruber et al., 2014; Gruber, Klimesch, Sauseng, & Doppelmayr, 2005; Klimesch et al., 2004). Gruber et al. (2014)

provided compelling evidence that for a given participant, the grand average P1 includes trials which do, and do not have positive-going alpha phase during the P1 time window. When there was negative going alpha phase in this time window, the P1 potential was not elicited in response to the stimulus, and behavioral responses to these stimuli were more delayed. This suggests that to obtain a true measure of the P1 component, trials with negative going phase during the P1 time window should be removed from the dataset.

In the present paper, we apply this logic to ERPs acquired during the Poffenberger paradigm by firstly analysing IHTT in distinct alpha and theta frequency bands (since these are the frequencies of interest for the P1 and N1 components) and secondly filtering out trials where the phase of the theta or alpha oscillation is in the opposite direction to that of the expected component (i.e. negative phase during the P1 time window; positive phase during the N1 time window). Our hypothesis is that, consistent with the preservation of the splenium in aging (Bastin et al., 2008, 2010; Hou et al., 2012; Madden et al., 2009; Salat et al., 2005), IHTT using this constrained ERP approach will be preserved in older adults to the level of young adults. We also calculated the CUD measure using the mean and median of the reaction time distributions to compare between young and older adults.

2. Method

2.1 Participants

Twenty-three healthy young adults (ages 18-27) and 32 healthy older adults (ages 63-80) participated in this study (see Table 1). All participants were right handed (self-reported) and had normal or corrected-to-normal vision, with no history of stroke or other neurological problems. Older adults were screened for Alzheimer-related memory impairment using the Memory Alteration Test (Rami, Molinuevo, Sanchez-Valle, Bosch, & Villar, 2007). No

participants were removed based on these scores. Chi-square tests indicated no significant differences between groups across sex, X^2 (1) = 0.09, p = .758. The groups did differ in terms of education, with older adults having slightly more years in education than young adults, t(54.98) = -2.22, p = .03.

Table 1 - Participant demographics

	Young (n = 23)	Older (n = 32)
Age	19.86 (2.15)	69.75 (4.91)
Years of Education	14.95 (2.01)	17.25 (4.50)*
Sex (M/F)	(7/16)	$(11/21)^{ns}$
M@T	-	45.87 (37-50; cut-off = 37)

*$p < .05$, ns = non-significant

2.2 Behavioral Paradigm

Participants were seated 57cm from a CRT monitor (1024x768 pixel resolution, 75Hz). A black fixation cross was positioned at the centre of a grey background. A 200Hz warning tone preceded a target stimulus by a pseudorandom interval of 500/750/1000ms. The target stimulus consisted of a black and white circular checkerboard with a diameter of 3° of visual angle. The target was presented 4° to the left or right of fixation cross (measured from the center of the fixation cross to the center of the target stimulus) for 50ms. The participant was instructed to fixate on the cross, and to quickly make a manual response by pressing a button with their index finger when they detected a checkerboard. A blank screen was presented between trials for either 1250/1500/1750ms to allow for the dissipation of ERP activity between trials.

Participants completed 330 trials of the task, divided into six blocks. Each block contained 25 stimulus presentations to the right (RVF) and left visual field (LVF) in a pseudorandom order. Five catch trials, in which no stimulus appeared, were also included to monitor the attention of the participant. In a given block, participants were asked to respond with a button press using either the left or right hand. The response hand alternated between blocks and the order was counterbalanced across participants. Fixation was monitored using a video-based eye tracker (Eyelink 1000; SR Research) recording at 1000Hz. Trials were rejected if the participant made a saccade outside of a 2x2 degree boundary centered on the fixation cross before they made a manual response.

2.3 Reaction time processing

Reaction times below 150ms and above three standard deviations of the single-subject mean RT were omitted from the data. We calculated the mean and median RT across the conditions of hand (left/right) and visual field (LVF/RVF). Raw CUD estimates were calculated by

subtracting the mean/median RTs from the uncrossed conditions ((LVF-left hand + RVF-right hand)/2) from the mean/median crossed RTs ((LVF-right hand + RVF-left hand)/2).

2.4 EEG acquisition and pre-processing

EEG was recorded via 64 electrodes on a cap, arranged in the international 10-20 system (Jasper, 1958), and amplified using NeuroScan Synampse^2 amplifiers (Compumedics). Bipolar vertical electrooculographic electrodes were placed above and below the center of the left eye. All leads were checked for proper contact with the scalp by ensuring that the direct current electrode offset was below 10kOhm. Activity was digitized on 24 bits with a sampling rate of 1024 Hz. EEG analysis was conducted using Matlab (Mathworks) and the EEGLAB toolbox (Delorme & Makeig, 2004). Channels were band-pass filtered offline between 1-30 Hz and down-sampled to 256 Hz. Channels containing spurious artefacts were identified by visual inspection and removed. Infomax independent component analysis (ICA) was used to remove eye movements and muscle artefacts from the data. Removed channels were interpolated using spherical spline interpolation. Before extracting epochs, the continuous data was bandpass filtered into the theta (4-8 Hz) and alpha (9-14 Hz) bands with a zero-phase IIR Butterworth filter using the *filtfilt* function in Matlab. Epochs were extracted from the data between -200ms and 700ms relative to stimulus onset and baseline corrected between -500 and 0ms. Trials that exceeded a ±75 μV amplitude threshold were rejected. The data was re-referenced to the common average and separated into LVF and RVF presentation conditions.

2.5 Data reduction and constrained ERP analysis

Our analysis of the EEG was restricted to two regions in the posterior right and left hemisphere, in which the P1 and N1 components are typically evoked. Electrode clusters from left (P3, P5, P7, PO5, PO7) and right hemispheres (P4, P6, P8, PO6, PO8) were

averaged to make two composite regions of interest (ROIs). Time windows of interest were defined for the detection of a P1 and N1 component. These were set liberally at 70-200ms for the P1 and 145-280ms for the N1. A custom Matlab script was used to identify trials that contained a negative peak in the contralateral ROI during the P1 time window or a positive peak during the N1 time window at either the alpha or theta frequency bands, and to mark and remove those trials from further analysis. The P1 and N1 peak latencies were calculated in the same time windows in each of the remaining trials (see Figure 1). Single-trial peaks were then averaged for each participant (see Figure 2 for an example). It is important to clarify that the ERP estimates of IHTT are independent of the crossed and uncrossed conditions of the CUD paradigm because visual transfer occurs automatically for every trial regardless of the manual response, and unlike the CUD, ERP-IHTT can be calculated on a single trial basis.

insert Figure 1 about here

insert Figure 2 about here

2.6 Data analysis

The reaction time data were analysed using a Condition (crossed/uncrossed) x Group (young/older) ANOVA with mean and median RTs as the dependent variables in separate models. The ERP latencies were analysed in Visual Field (LVF/RVF) x Hemisphere (left/right) x Group (young/older) ANOVAs for each of the alpha and theta frequency bands separately. For all ANOVAs, effect sizes are reported as generalized eta squared (ges; Bakeman, 2005) whereby an effect of 0.02 is considered small, 0.13 medium, and 0.26 as large. For the ANOVA models conducted on ERP latencies, post-hoc t-tests with Bonferroni-Holm adjustments for multiple comparisons were carried out between groups at each

combination of the Visual Field and Hemifield factors (e.g. left hand LVF; left hand RVF; right hand LVF; right hand RVF).

3. Results

3.1 Behavioral data

On average, 3% of trials were removed due to eye movements away from fixation during stimulus onset. The cut-off criteria for reaction times resulted in the omission of 0.06% of trials on average. The remaining number of RT trials across all participants was 295.6 (SD = 2.97).

For mean RT, the main effect of Group was significant, $F(1,53) = 12.43$, $p < .000$, $ges = 0.20$, indicating that older adults had significantly slower reaction times than young adults. There was a significant main effect of Condition, $F(1,53) = 18.89$, $p < .000$, $ges = 0.003$, which demonstrated that RTs to the stimulus ipsilateral to the response hand were quicker than RTs to the contralateral stimulus. In other words, the uncrossed RTs were quicker than the crossed RTs, as is traditionally observed. Crucially, there was no interaction between Group and Condition, $F(1,53) = 0.008$, $p = .927$, $ges < 0.00$, suggesting that the difference between crossed and uncrossed RTs did not vary across groups. The mean CUD value for younger adults was 4.6ms (SD = 7.11) and the mean CUD value for older adults was 4.47ms (SD = 8.37; see Figure 3A).

For median RTs, there was a significant main effect of Group, $F(1,53) = 10.51$, $p = .002$, $ges = 0.17$, and a significant main effect of Condition, $F(1,53) = 35.12$, $p < .000$, $ges = 0.003$, in the same directions as the mean RT results. No significant Group by Condition effect was observed, $F(1,53) = 0.07$, $p = .788$, $ges < 0.00$. The median CUD value for young adults was

-4.47ms (SD = 5.11) and the median value for older adults was -3.98ms (SD = 5.51; see Figure 3B).

insert Figure 3 about here

3.2 P1 analysis

On average, 243 trials per participant were included in the ERP analyses after cleaning the data (SD = 38, Range = 143-299). A Group x Visual Field x Hemisphere ANOVA was conducted for P1 latencies in both the theta and alpha bands. In the theta band, the typical Hemisphere x Visual Field interaction was present, $F(1,53) = 128.41$, $p < .000$, *ges* = 0.37, suggesting that contralateral latencies were quicker than ipsilateral latencies, such that interhemispheric transfer had occurred. There was a significant three-way interaction, $F(1,53) = 14.96$, $p < .000$, *ges* = 0.06, suggesting that the groups differed in terms of the Visual Field x Hemisphere interaction. A series of post-hoc Bonferroni-Holm adjusted t-tests were conducted to test for group difference at each level of Hemisphere and Visual Field. There were no differences between groups in P1 latencies at the ipsilateral hemisphere for either the LVF (adjusted $p = .5$) or RVF conditions (adjusted $p = 1$). In the contralateral hemispheres, older adults had significantly quicker latencies in both the LVF (adjusted $p = .005$) and RVF conditions (adjusted $p < .000$), suggesting that older adults had significantly quicker P1 ERPs in the receiving hemispheres, but not in the transferred hemispheres.

For the alpha band, the Group x Visual Field x Hemisphere interaction approached significance, $F(1,53) = 3.699$, $p = .060$, *ges* = .02. We again tested for group differences at each combination of visual field and hemisphere using t-tests. Older adults had significantly quicker P1 latencies in the hemisphere ipsilateral to the RVF stimulus (adjusted $p = .008$), while a similar trend was evident for latencies in the hemisphere ipsilateral to the LVF

stimulus (adjusted p = .057). In the contralateral hemispheres, there were no group differences for either the LVF (adjusted p = 1) or RVF stimulus (adjusted p = 1). Older adults therefore exhibited quicker alpha P1 latencies in the transferred hemisphere (see Figure 4).

insert Figure 4 about here

3.3 N1 analysis

The Group x Visual Field x Hemisphere interaction was significant for N1 latencies in the theta band, $F(1,53) = 19.18$, $p < .000$, *ges* = .06 (see Figure 5). At the ipsilateral hemispheres, there were no significant group differences for the LVF (adjusted p = 1) or RVF conditions (adjusted p = .96). Group differences were also absent in the hemisphere contralateral to the LVF stimulus (adjusted p = 0.29). For the hemisphere contralateral to the RVF stimulus, older adults had significantly quicker N1 latencies (adjusted p = .001). In the alpha band, the three-way interaction did not approach significance, $F(1,53) = 0.98$, p = .326, *ges* = .004, and so no post-hoc tests were conducted.

insert Figure 5 about here

4. Discussion

This study aimed to test whether interhemispheric transfer is affected in older age. Using a constrained ERP approach, we calculated IHTT from peaks arising during the P1 and N1 time windows which were filtered into either the theta or alpha frequency bands. We assumed that because CC splenium fibres connecting visual areas are spared in healthy aging (Bastin et al., 2008, 2010; Hou et al., 2012; Madden et al., 2009; Salat et al., 2005), IHTT as measured by visual ERP components would not differ between young and older adults. We

also calculated the classic CUD measure by subtracting RTs in the uncrossed (ipsilateral response) from the crossed (contralateral response) conditions. Since there is still debate surrounding which channels of the CC are responsible for the CUD, we had no concrete hypothesis about how aging should affect the CUD. If the CUD operates through the CC genu, we should observe an elongated CUD in older adults, who experience degeneration of genu fibres with advancing age (Bastin et al., 2008, 2010; Hou et al., 2012; Madden et al., 2009; Salat et al., 2005). If the CUD is related to midbody or splenium fibres, there should be no difference between young and older adults.

No age differences in the CUD

There was no detectable difference in CUD estimates between young and older adults on average. This supports the findings of Linnet & Roser (2012) and Schulte et al., (2013) but contradicts the findings of many others (Bellis & Wilber, 2001; Davis et al., 2012; Jeeves & Moes, 1996; Reuter-Lorenz & Stanczak, 2000). The absence of the effect cannot be attributed to the relative youth of the older adults in this study, as Bellis & Wilber (2001) reported that adults as young as 55-60 had longer CUDs compared to 35-45 year olds. Our data suggest that transfer measured by the CUD is likely associated with callosal fibres that do not experience degeneration during healthy aging, such as the midbody fibres. As mentioned, Iacoboni & Zaidel (2004) found that the CUD correlated more strongly with BOLD activity from the superior parietal cortex than with other areas of activation during their fMRI study, in support of this theory. Additionally, it is compatible with the BOLD activation in the CC midbody during the Poffenberger paradigm (Gawryluk et al., 2010b). It is, however, incompatible with the observed activation of the CC genu during the task (Gawryluk et al., 2010a; Omura et al., 2004; Tettamanti et al., 2002; Weber et al., 2005), suggesting that while the vascular properties of the genu may be involved in Poffenberger-derived transfer, it may not by crucial for the CUD.

There are other potential explanations for the lack of age differences. Iacoboni & Zaidel (2000) reported that thousands of trials are required to obtain CUD values that reflect true callosal transfer, whereas this study, among others, reported a CUD based on 300 trials. However, Bellis & Wilber (2001) used 320 trials and still reported effects of aging, deeming it unlikely that the discrepancy of between-group effects between our study and others can be solely attributed to the increased variability associated with having an insufficient number of trials. Furthermore, our sample size was comparable to that of other studies who reported an age effect (Jeeves & Moes, 1996; Bellis & Wilber, 2001, Reuter-Lorenz & Stanczak, 2000) suggesting that the power to achieve a between-groups effect was sufficient. We demonstrated that our results were consistent across the mean and median measures of central tendency, the median often being the choice of central tendency for RTs (Bellis & Wilber, 2001; Jeeves & Moes, 1996). Alternatively, the CUD may be sensitive to individual differences and variations in the task design, such as stimulus size, duration or eccentricity, which often vary between studies. It is possible that certain presentation parameters utilised in other studies are more sensitive to aging. Lastly, older adults had a significantly higher level of education than young adults in the present study, which may have reduced the likelihood of detecting a difference in the CUD between young and older adults. While the effect of education on the CUD has not been directly investigated, some studies have associated CC integrity with higher callosal integrity (Luders et al., 2007; Penke et al., 2010), suggesting a possible preservative effect on IHTT for older adults with higher levels of education. However, we acknowledge that level of education is a crude measure of cognitive ability and further research needs to be conducted to rule out the effects of cognitive ability on transfer speed. Nevertheless, from the data presented here we draw the conclusion that interhemispheric transfer as measured by the CUD is spared in older adults, and likely operates through the CC midbody, which is unaffected by aging.

Age differences in ERP-IHTT

Our ERP analysis deviated from the traditional method of picking latency peaks from the single-subject grand average waveforms. This was possible by considering specific frequency bands of interest, namely the theta and alpha bands, in which the P1 and N1 components are situated according to a large body of literature (Freunberger et al., 2008; Gruber et al., 2014, 2005; Klimesch et al., 2004). In each of the analyses presented here, the typical Visual Field x Hemisphere interaction was highly significant with a large effect size, indicating that interhemispheric transfer was taking place between lateralized visual ERPs in both frequency bands. For both the P1 and N1 components in the theta band, the crucial Group x Visual Field x Hemisphere interaction was present, suggesting that older adults were associated with an elongated IHTT. Surprisingly, this effect was driven by quicker P1 latencies in the hemisphere contralateral to the stimulus, rather than elongated ipsilateral peak latencies in the older adult group. These findings suggest that visual information processing in the theta band is taking place more quickly in older adults than in younger adults, while the transferred signal in older adults reaches the ipsilateral hemisphere at around the same time as young adults. While this presents as an elongated IHTT in older adults, there is not necessarily an advantage for a quicker IHTT in younger adults since the transferred signal reaches the ipsilateral hemisphere at the same time. This calls into question the validity of ERP IHTTs for measuring age-related decline, if aging is associated with a shortening of the contralateral peak latency. A quickening of P1 or N1 latencies has not typically been reported for older adults (Curran et al., 2001; Emmerson-Hanover, Shearer, Creel, & Dustman, 1994; Hoptman, Davidson, Gudmundsson, Schreiber, & Ershler, 1996; Onofrj, Thomas, Iacono, D'Andreamatteo, & Paci, 2001). We therefore assume that our finding of such is a result specific to the theta band, since the effect was not present for alpha band peaks. Further

research on visual EEG responses in specific frequency bands will be necessary to uncover whether this effect is robust across different samples.

The pattern of results seen in the theta band results was not observed in the alpha band peaks. In fact, there was a trend towards an elongated P1 IHTT in younger adults compared to older adults, which was driven by delayed ipsilateral latencies in the young adults, rather than a reduction in contralateral latencies as observed in the theta band for older adults. Although this effect was weaker than those observed in the theta band, IHTT driven by elongated ipsilateral latencies, rather than shortened contralateral latencies, is a more conceptually valid manifestation of IHTT. Our results therefore suggest that older adults do not experience an elongated transfer in the alpha band, and that they may even be reduced compared to young adults.

Conclusions and future directions

From the results of this study we conclude that interhemispheric transfer as measured by the Poffenberger paradigm is not affected in older adults. Our results largely map on to the many studies that have documented age-related structural change in the CC (Bastin et al., 2008, 2010; Hou et al., 2012; Madden et al., 2009; Salat et al., 2005), which suggest that only the genu of the CC experiences degeneration with advancing age. We have demonstrated that functions governed by the preserved sections of the aging CC are unaffected in older adulthood. Functional measures of the posterior CC could be an important measure for tracking changes in the aging brain that may deviate from the trajectory of normal development. For example, lower splenium integrity has been linked to increases in hypertension in older adults (Wong, Ma, & Lee, 2017b), which in turn is associated with increased risk of coronary heart disease and cardiovascular problems later in life (Rigaud & Forette, 2001).

Additionally, structural imaging studies have suggested that the CC splenium may be more specifically targeted than other regions by Alzheimer's dementia (AD) pathology (Fletcher et al., 2016; Genc et al., 2016; Hanyu et al., 1999; Hoy et al., 2017; Madhavan et al., 2015; Sandson, Felician, Edelman, & Warach, 1999; Xiaoying Tang, Qin, Zhu, & Miller, 2017). The CUD may not be an appropriate measure of functional decline of the CC in AD, as equivalent performance in AD and control groups has been demonstrated previously (Reuter-Lorenz & Mikels, 2005). Functions of the splenium, such as ERP-derived IHTT, may be a useful marker for structural decline in AD as they are independent of aging effects. Functional measures of structural integrity that are resistant to age effects are highly desirable for clinical assessment of age-related disorders (Logie, Parra, & Della Sala, 2015). To our knowledge, ERP-IHTT in AD and its preclinical or prodromal stages has not yet been investigated.

From a methodological point of view, we consider the constrained ERP approach extremely useful for measuring IHTT, as it filters out trials in which the P1 and N1 ERPs were not elicited, and therefore avoids conflating the morphology of the single-subject average with noisy trials. The development of this easily replicable approach highlights the need for synthesis between the ERP and EEG oscillation literatures, in order to avoid the issues associated with traditional ERP methods.

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Figure captions

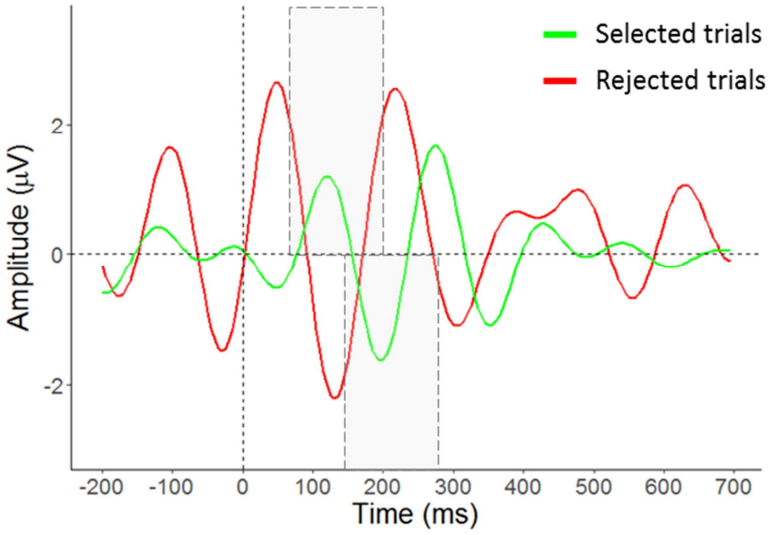
Figure 1. Illustration of the constrained ERP approach. Trials with negative going deflections in the P1 time window (70-200ms) and positive-going deflections in the N1 time window (145-280ms) were removed from the data of each subject. The red line reflects the mean signal from rejected trials in one example participant. The green signal represents the mean of the trials selected for analysis. For a similar approach see Gruber et al. (2014).

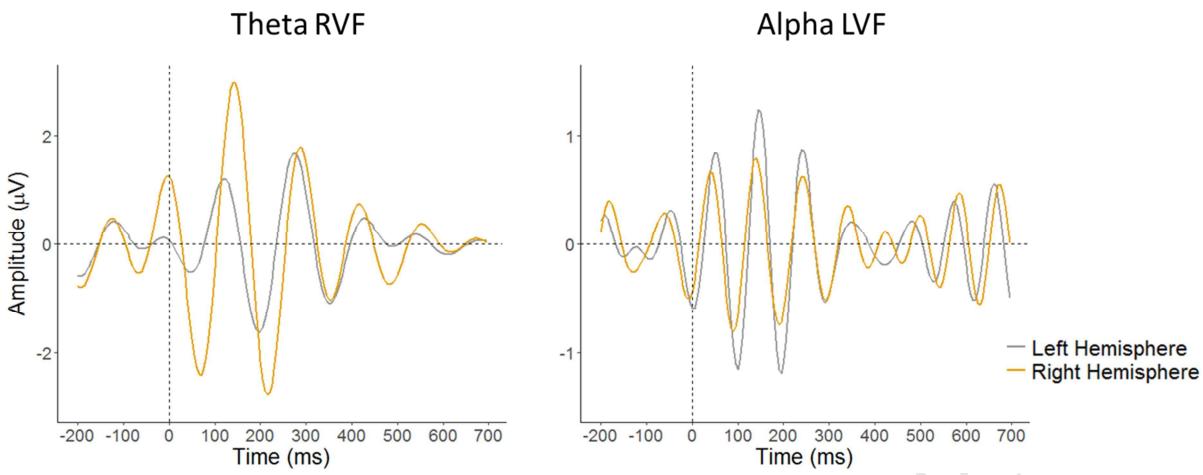
Figure 2. Examples of interhemispheric transfer in the theta and alpha bands in a single older adult participant. **A:** RVF stimulation with earlier theta P1 and N1 peaks in the left hemisphere. **B:** LVF stimulation with earlier alpha P1 and N1 peaks in the right hemisphere.

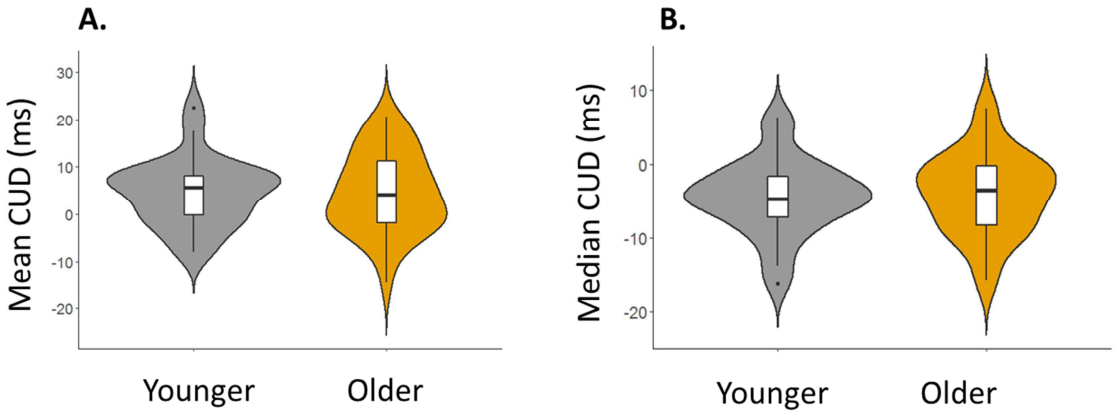
Figure 3. Violin boxplots illustrating the distribution of CUD estimates in young and older adults as calculated by the mean (A) and median (B) RTs. The bold horizontal line represents the median of the CUD distributions, while the box edges represent the interquartile range. The whiskers represent 1.5 times the upper and lower quartile, and dots represent outliers.

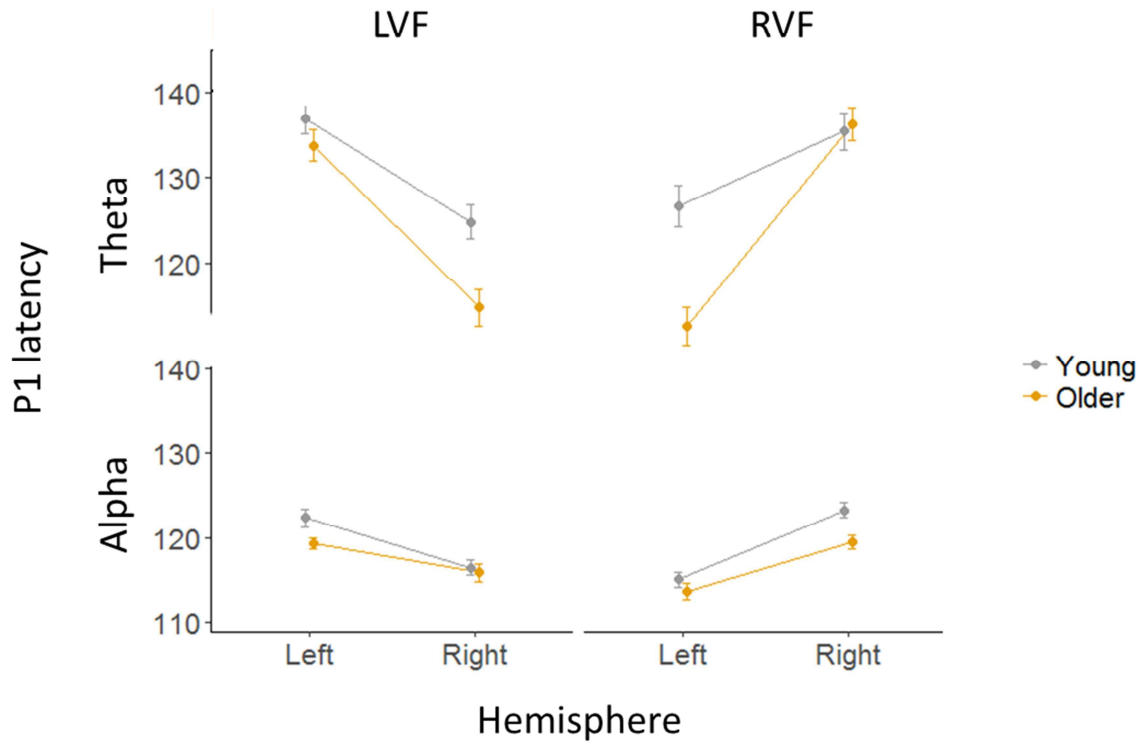
Figure 4. P1 latencies in the theta and alpha bands across the levels of Group, Visual Field and Hemisphere. Error bars indicate the standard error of the mean.

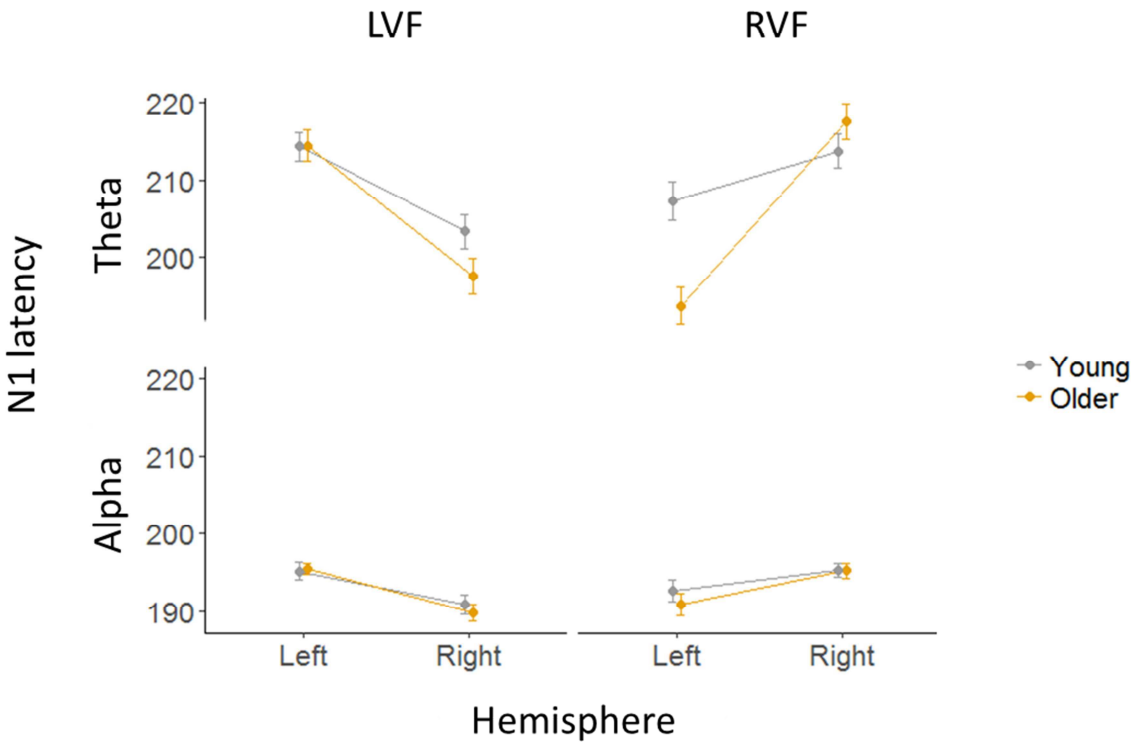
Figure 5. N1 latencies in the theta and alpha bands across the levels of Group, Visual Field and Hemisphere. Error bars indicate the standard error of the mean.








LVF
RVF
Theta
Alpha
P1 latency
140
130
120
110
Left
Right
Hemisphere
Young
Older


LVF
RVF
N1 latency
Theta
Alpha
220
210
200
190
Left
Right
Hemisphere
Young
Older

- Interhemispheric transfer time is measured using the crossed-uncrossed difference and a constrained ERP approach
- The crossed-uncrossed difference did not differ between young and older adults
- Older adults exhibited a shortening of the contralateral ERPs in the theta band
- ERP transfer in the alpha band was equivalent between young and older groups
- Functions of the posterior corpus callosum are not altered in older age