Cortical Phase Shifts in Subjective Cognitive Impairment at 7 Tesla

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Target Audience: Clinicians.

Introduction: Both postmortem and in vivo studies have indicated the potential of ultra-high field magnetic resonance imaging (MRI) in visualizing iron-related changes in the cerebral cortex of patients with Alzheimer's disease (AD) [1]. The accumulation of Alzheimer-associated pathology has been known to precede clinical symptoms by as much as two decades [2]. Subjective cognitive impairment (SCI) has been suggested as a manifestation of AD preceding mild cognitive impairment [3]. The main aim of this study was to investigate whether cortical phase shifts on T2*-weighted MRI at 7T, possibly implicating the deposition of Aβ plaques, can be detected in subjects with SCI. The secondary aim was to investigate which parts of the neuropsychological spectrum are associated with cortical phase shifts.

Methods: Scanning was performed in 28 AD patients (18 male/10 female, mean age 71.2 years), 18 subjects with SCI (13 male/5 female, mean age 66.5 years), and 27 healthy control (HC) subjects (16 male/11 female, mean age 69.0 years). This study was approved by the local institutional review board. Written informed consent was obtained from all subjects. Participants were scanned at 7T using a 2D flow-compensated transverse T2*-weighted gradient-echo scan with a spatial coverage of 22 mm, including the frontal and parietal regions, with a total imaging duration of 10 minutes. Imaging parameters were: repetition time/echo time 1764/25 ms, flip angle 45°, slice thickness 1.0 mm with a 0.1 mm interslice gap, 20 slices, 240 x 180 x 22 mm field of view, 1024 x 768 matrix size; resulting in an in-plane nominal spatial resolution of 0.24 x 0.24 mm^2.

All MRI scans were scored quantitatively by measuring cortical phase shifts of the frontal, parietal, and left and right temporoparietal regions. The overall peak-to-peak phase shift between cortical gray and subcortical white matter was calculated for each region and the whole brain in each subject. In addition to scanning, participants were subjected to a standard neuropsychological test battery including a Mini Mental State Examination (MMSE), Cambridge Cognitive Examination (CAMCOG), Wechsler Memory Scale (WMS), Trail Making Test (TMT), a Stroop test, and a Geriatric Depression Scale (GDS). Post-hoc Mann–Whitney U tests were used to assess differences in phase shifts between groups. Linear regression analysis was performed to determine the association between the different neuropsychological tests and phase shift in the cortex, adjusted for age and gender. This was also performed with the phase shift divided into tertiles.

Results: Cortical phase shifts in subjects with AD were all significantly ($p<0.001$) greater than in subjects with SCI and HC. Cortical phase shifts in SCI were not increased compared to HC. Highly significant ($p<0.001$) correlations, adjusted for age and gender, were found between cortical phase shifts and MMSE, CAMCOG, WMS, TMT part B and Stroop part 2, and a significant correlation between TMT part A ($p=0.001$) and Stroop part 3 ($p=0.030$) and cortical phase shifts (table 1). No differences were found between groups on the depression scale (GDS). Figure 1 shows the plot of tertiles of cortical phase shifts with mean MMSE and CAMCOG scores. This plot shows that subjects with a large cortical phase shift demonstrate significantly reduced MMSE and CAMCOG ($p<0.001$) scores.

Table 1. Correlation between cortical phase shifts and scores on different neuropsychological tests, corrected for age and gender.

	β	p-value
MMSE	-0.711	**0.000**
CAMCOG	-0.766	**0.000**
WMS	-0.641	**0.000**
TMT part A	0.422	**0.001**
TMT part B	0.695	**0.000**
Stroop part 2	0.554	**0.000**
Stroop part 3	0.372	**0.030**
GDS	0.101	0.597

Discussion and Conclusion: Increased cortical phase shifts were measured in AD subjects compared to healthy control subjects. No such changes were found for subjects with SCI. Our data show that although increased cortical phase shifts at high field are associated with poorer cognitive performance, especially in the executive domain, in subjects with SCI no AD-like MRI phase changes could be determined.

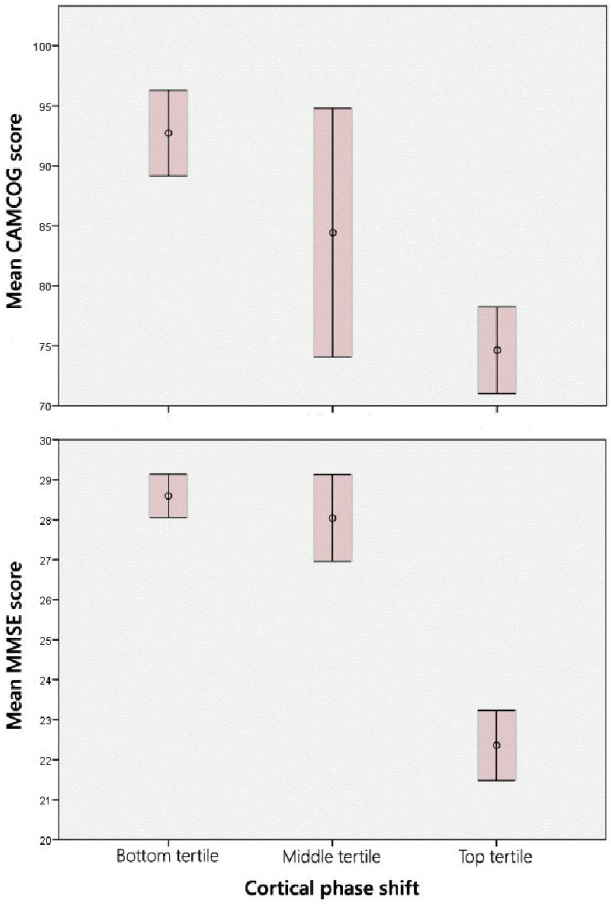

Fig 1. Plots of tertiles of cortical phase shifts with mean CAMCOG and MMSE scores (Error bars = 95% CI).

References: [1] Van Rooden S et al. (2013) Alzheimer's & Dementia in print. [2] Jack C et al. (2010) Lancet Neurology: 9:119-128. [3] Striepens N et al. (2010) Dementia and Geriatric Cognitive Disorders 29, 75-81.