Age related changes in DTI of the brain white matter associated with EEG measures

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Introduction

Electroencephalographic (EEG) studies of aging have shown prolongation and diminution of evoked potential (EP) components. Typically, the magnitude of a EP signal at the scalp is slower and in some instances also smaller. Changes in the EP signal in aging have been interpreted as dedifferentiation or widespread activation related to compensatory mechanisms activating additional resources. It has been hypothesized that the slowing of the EP components can be attributed to processing delay. DTI, on the other hand, showed that with aging there is significant decrease in anisotropy accompanied by increased diffusivity (1). Here we are testing the relationship between the visual motion onset EPs and integrity of WM as measured by DTI, expecting that changes in WM (increased diffusivity, decreased anisotropy) will be correlated with the EP processing diminution.

We previously reported optic flow EP as parietal negative waves peaking around 200 msec after onset of patterned visual motion (N200) (2). Here we are using the visual EP responses to the radial motion reversal stimuli and combining them with DTI measures of fractional anisotropy (FA) and diffusivity (<D>) to evaluate age effect on the cross-property relationship between the brain electrical activity and brain integrity of WM.

Methods

We performed DTI and EEG on 11 healthy older adults (OA) (mean age = 75.6, age > 60) and 11 younger normals (YN)(mean age = 35.4, age < 60).

Electroencephalographic recordings : We presented alternating patterns of inward and outward radial optic flow, randomly varying the stimulus duration from 1.25s, 2.5s, and 5s. YN and OA subjects maintained centred visual fixation monitored by infrared eye-tracking. We recorded EPs from 32 channels Neuroscan EEG with linked-ears reference. The EEG signals were low-pass filtered at 100 Hz, sampled at 500 Hz. Here, we present only results from vertex electrodes (FCz, Cz, CPz, PZ, and Oz).

DTI protocol: MRI examinations were performed on a GE Signa 1.5 T MR scanner (LX9.1). In addition to conventional anatomic images, coronal DTI imaging with a single-shot pulsed-gradient spin-echo (PGSE) EPI were performed. Diffusion weightings were applied in 20 different orientations with b value = 0 and 1000 s/mm^2. TR/TE = 8000/85ms, FOV22cm, and matrix128X128. We used 22 contiguous slices perpendicular to the genu-splenium line, approximately 7mm thick, covering WM from the subcortical frontal to posterior parietal and occipital areas. The DTI images were processed using home-built software.

Image analyses: fractional anisotropy (FA), and diffusivity (<D>), were calculated for 9 regions of interest (ROI): I. Subcortical WM in the prefrontal region and in the parietal-temporal region; II. Corpus Callosum (CC): at the anterior (A), middle (M) and posterior (P) sites; III. Limbic System Fibers: bilateral cingulum; IV. Association fibers: Superior Longitudinal Fasciculus-SLF.

Results

1. **EEG results**: YN subjects showed significantly higher P200 amplitudes than the OA subjects. YN subjects had also ~ significantly faster EPs than OA subjects: P100 (25 ms, p=.001), N200 (25 ms, p=.002), and P200 (20 ms, p=.03)(Fig 1).
2. **DTI results**: YN subjects showed significantly higher FA at middle CC ($p < .05$), and significantly smaller <D> at all ROIs ($p < .01$) than OA subjects (Fig 2).
3. **Relationship between EEG and DTI measures**: We used bivariate correlational analyses to determine which EEG measures from the vertex electrodes (FCz, Cz, CPz, Pz, and Oz) would correlate with DTI measures. At the anterior and central sites we found significant correlations between <D> at SUB-A and P200 amplitude at FCz (r = -.53, p=.01), and significant correlations between FA at SUB-A and latencies for P100, N200, at CPz (r=--.58, p=.004, r=-.55, p=.009, respectively), and SUB-A and P200 latencies at FCz (r=-.57, p =.006) (Fig3B). There was also a significant correlation between <D> at the anterior CC and P200 latencies at central site CPz (r=.47, p =.04). At the posterior sites we found significant correlations between FA at SUB-P and P100 amplitude at Oz (r=.46, p =.03), between <D> at CIN-P and N200 amplitude at Pz (r=.57, p=.005), between <D> at SLF-P and N200 amplitude at Pz (r=.52, p=.01)), between <D> at SUB-A and P200 amplitude at Pz (r=-.51, p=.02) (Fig3A), and between <D> at SLF-P and P200 amplitude at Pz (r=-.47, p =.03). For EP latencies, there was only one significant correlation at the posterior sites: <D> at SUB-P was significantly correlated with P200 latency at Pz (r=.50, p=.02) and Oz (r=.43, p=.04). Overall, WM integrity at anterior sites was more correlated with latencies of motion reversal EPs whereas WM integrity at the posterior sites was more correlated with amplitudes of motion reversal EPs.

Fig1 **Fig2** **Fig3A** **Fig3B**

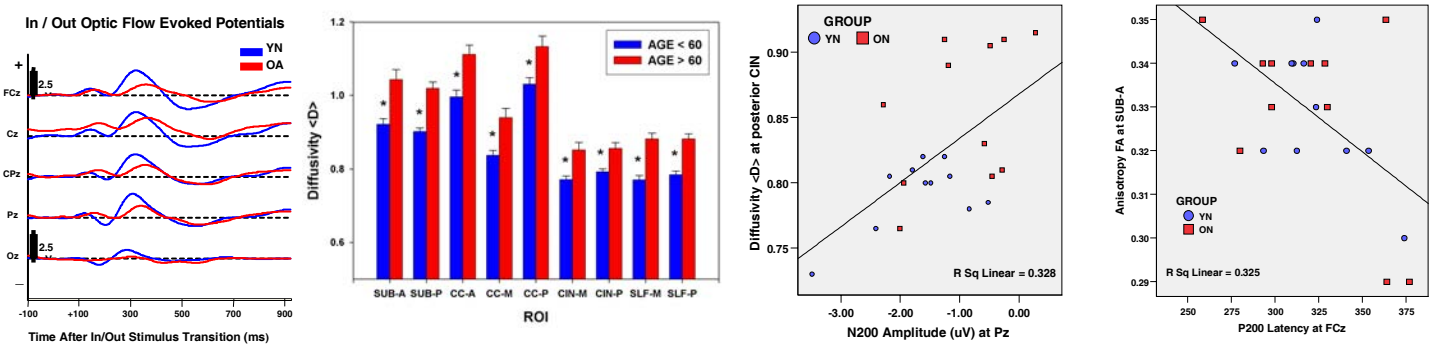

Fig 1 Waveforms of EEG evoked responses to alternating optic flow for younger normals (YN) – blue, and older adults (OA) – red. **Fig 2**. Bar graphs representing average <D> for YN and OA subjects from all ROIs. **Fig 3(A)** Scatter plot of correlation between N200 amplitude at Pz and <D> from posterior cingulum (CIN). **Fig 3(B)** Scatter plot of correlation between P200 latency at FCz and FA from anterior subcortical WM (SUB-A).

Discussion

Alternating optic flow yielded robust EPs in both groups, however OA subjects showed prolonged latencies for ~ 25 msec across all EP components and also significantly diminished late P200 component amplitude. In other words, increasing age can be linked to overall slowing of EP responses and smaller P200s amplitudes. Aging was also linked to decreased anisotropy of the body of the CC and increased diffusivity of WM in all ROIs. Linked together, decreased amplitudes of motion reversal EP components were associated with increased diffusivity primarily from posterior brain regions, while increased latencies of motion reversal EP components were associated with decreased anisotropy primarily from anterior brain regions. Increased diffusivity could result from an increase in extracellular space possibly due to demyelination. Changes in extracellular space and/or in the axons could be also involved in the correlation between increased diffusivity and decreased EPs amplitudes as well as in the correlation between decreased anisotropy and increased EP latencies. Based on the above results we hypothesize that the portion of the processing diminution can be attributed to slowing of the transfer of neuronal code due to axonal and WM alterations and/or loss of small myelinated fibers.

Reference: (1) O'Sullivan et al., Neurology, 57, 623-638 (2001); (2) Kavcic et al., Brain, 126, 1173-1181 (2006).