Effects of aging and gender on brain intrinsic functional connectivity: a resting state study in a large cohort of healthy subjects

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Purpose. Aim of this study was to analyze gender- and age-related effects on resting state (RS) functional connectivity (FC) within and among RS networks (RSN) with potential functional relevance in a large cohort of healthy subjects. Previous studies have demonstrated a decreased brain RS FC with aging [1]. Moreover, differences of RS FC have been shown between men and women [2]. However, the combined effects of aging and gender on RS FC have not been investigated yet.

Methods. RS fMRI and 3D T1-weighted scans were acquired from 285 right-handed healthy controls (148/137 men/women, range=8-79 years). Independent component analysis [3] and a template-matching procedure were used to identify functionally relevant RSNs. The Functional network connectivity (FNC) toolbox [4] was used to assess significant functional connectivity among networks. SPM8 and ANCOVA models were used to assess correlations of RS FC with aging in men and women, corrected for regional gray matter volume. Effects of aging and age-by-gender interactions on connectivity among networks were also assessed.

Results. The sensorimotor and auditory networks showed a distributed pattern of FC decrease with aging in both genders. Conversely, age-related changes in visual networks were relatively modest. In the default mode network, FC changes of the parietal lobe were detected, whereas FC changes in the salience and executive networks mainly involved the frontal lobe. In the working memory networks, there was an ipsilateral decrease and contralateral increase of RS FC with aging. In the attention network, parietal FC changes were more evident in men than in women. FNC was mainly increased with aging in both genders (Figure). There was a prevalent involvement of the sensory and the attention networks in men; and a prevalent involvement of the sensory and working memory networks in women.
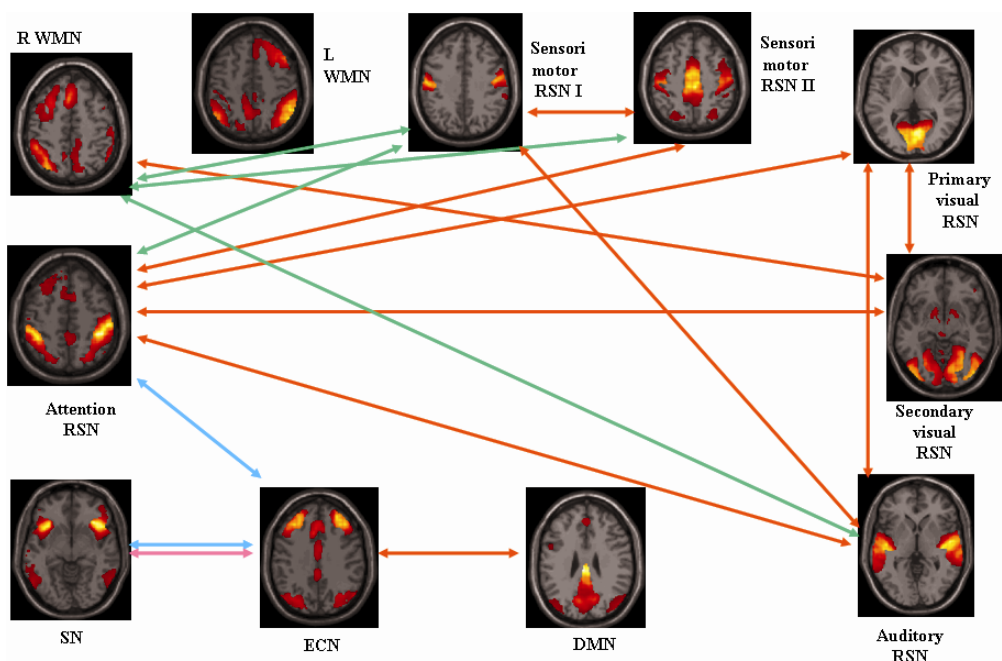

Figure legend.
Diagram showing resting state networks having a significantly different pair-wise connectivity with aging.
Red arrows: increased connectivity with aging in men.
Green arrows: increased connectivity with aging in women.
Blue arrows: decreased connectivity with aging in men.
Pink arrows: decreased connectivity with aging in women.

Discussion and conclusions. Vulnerability to aging was detected in almost all RSNs with potential functional relevance. However, age and gender effects were variable across networks. Our results might contribute to the understanding of gender-related differences in the pathobiology of aging.

References. [1] Biswal B, et al. PNAS 2010;107:4734-4739. [2] Filippi M, et al. Hum Brain Mapp 2012; doi: 10.1002/hbm.21514. [3] Calhoun V, et al. Hum Brain Mapp 2001;14:140-151. [4] Jafri M, et al. Neuroimage 2008;39:1666-1681.