Structural and functional connectivity changes in the brain associated with shyness but not with social anxiety

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**Target audience:** Psychologist; Psychiatrist; Radiologist; Neuroscientist

**Introduction:**
How to distinguish shyness from social anxiety and trait anxiety has been of great concern to both clinicians and researchers. Shyness is generally considered to be a normal personality trait, whereas social anxiety is viewed as a potential clinical disorder in DSM-IV. Nevertheless both of these conditions share many symptoms, including somatic, behavioral and cognitive symptoms (1), and this raises the question about the diagnostic boundaries for social anxiety. Furthermore, shyness and social anxiety are associated with hyper-responsivity to social stimuli in both the frontal cortex and limbic system (2, 3). However, to date no studies have investigated whether common structural differences in the brain may contribute to both these two and if they result in altered functional connectivity. We have addressed this issue by using voxel-based structural MRI (sMRI) and resting state functional MRI (fMRI) to test correlations between brain structure, functional connectivity and shyness and social anxiety.

**Methods:**
We examined 61 healthy adult subjects for their shyness (Cheek and Buss Shyness scale), social anxiety (Liebowitz social anxiety scale) and trait anxiety scores. All participants were interviewed with the Structured Clinical Interview for DSM-IV to exclude psychiatric disorders, especially anxiety disorder. The sMRI and fMRI scan were acquired on a whole-body 3.0 T Siemens MR scanner with a 12-channel head coil. The sMRI data processing was carried out using DARTEL to calculate the parametric maps of grey and white matter density, whereas the fMRI data processing was conducted by DPARSF software to calculate the parametric maps of functional connectivity. Voxel-based morphometric analysis and seed-based functional connectivity analysis were then employed to investigate structural and resting-state functional connectivity properties, respectively. Stepwise multiple regression models were used to estimate specific shyness and social anxiety correlations.

**Results:**
As expected we found that shyness scores were correlated to some degree with those for social anxiety ($r = 0.38; p = 0.003$). Our findings revealed that shyness was positively correlated with grey matter density changes in the cerebellum posterior lobe, bilateral superior temporal gyrus and parahippocampal gyrus, and the right insula (at a cluster level with FWE corrected at $p < 0.05$). Functional connectivity correlations with shyness scores were found in connections between the superior temporal gyrus, parahippocampal gyrus and the frontal gyri, between the insula and precentral gyrus and inferior parietal lobule, and between the cerebellum and precuneus (with Alpha sim corrected combined height threshold of $p<0.001$ and minimum cluster size of 24 voxels). Additional correlations were found for amygdala connectivity with the medial frontal gyrus, superior frontal gyrus and inferior parietal lobule despite the absence of any structural correlation. By contrast no structural and functional connectivity measures correlated significantly with social anxiety or trait anxiety scores.

**Discussion & Conclusions:**
Our findings provide the first evidence that shyness is specifically associated with structural and functional connectivity changes in cortical and limbic regions involved with processing social stimuli. Thus the shyness trait has both structural and functional underpinnings in the brain. Interestingly, these associations were not found with social or trait anxiety scores in healthy individuals despite both having some behavioral correlation with shyness. Our results therefore provide objective evidence for differences between shyness and social and trait anxiety in terms of brain alterations, and demonstrate the importance distinguishing between them in both healthy and clinical populations.