Imaging Parameters

Each session began with the acquisition of high-resolution T1-weighted 3D anatomical images using a 3D Magnetization Prepared Rapid Gradient Echo (MP-RAGE) sequence (TR = 23ms, TE = 2.98ms, Slice Thickness = 1mm, Image Matrix = 256 x 256, Flip Angle = 30 degrees, FOV = 256mm, interleaved excitation). This was followed by fMRI acquisitions with T2* weighted gradient echo (GE) echo-planar images (EPI) for blood oxygenation level dependent (BOLD). Functional images, using T2* weighted gradient echo (GE) echo-planar imaging (EPI) sequence images were acquired for the blood oxygenation level dependent (BOLD) functional MRI measurements. The following parameters were used for gait imagery fMRI: TR = 3000ms, TE = 30ms, flip angle: 90°, slice thickness = 4mm, in-plane resolution = 4 x 4 mm, FOV = 256mm, 64 x64 image matrix, number of slices: 38, interleave excitation. The parameters for the working memory fMRI were: TR = 3000ms, TE = 30ms, flip angle: 90°, slice thickness = 4mm, in-plane resolution = 2.34 x 2.34 mm, FOV = 300 mm, 128 x128 image matrix, number of slices: 37, interleaved excitation. Diffusion tensor imaging (DTI) data was obtained with the following parameters: TR = 8240ms, TE = 88ms; FOV = 256mm; slice thickness = 2mm, no gap; 64 axial slices. Diffusion was measured along 99 non-

collinear direction using b-value of 1000 s/mm^2 and 10 images with no diffusion weighting (b_0=0s/mm^2).

Functional MRI analyses

All fMRI data were first processed using an in-house software package fmr_preprocess. The steps included motion correction by realigning all functional volumes to the third volume of that run. The images were then spatially smoothed with a 6-mm full-width at half-maximum Gaussian filter to increase the signal-to-noise ratio of the data, the tolerance of the subsequent analysis steps to residual motion in the scans, and to minimize resampling artefacts. Following image processing, a voxel-wise statistical analysis comparing activity during each experimental task condition against the control task condition (i.e. baseline) was then performed using fMRIstat [24]. A design matrix of the linear model containing the onset time and duration of each task condition was convolved with a hemodynamic response function modeled as a difference of two gamma functions, and corrected for slice-timing to coincide with the acquisition of each slice [30]. Temporal and spatial drifts were removed by modeling them as an autoregressive process of degree 1. At each voxel, the autocorrelation parameter was estimated from the least squares residuals using the

Yule-Walker equations, after a bias correction for correlations had been induced by the linear model. The autocorrelation parameter was first regularized by spatial smoothing, and then used to whiten the data and the design matrix. Then, the linear model was re-estimated using least squares on the whitened data to produce estimates of effects and their standard errors. Data from each individual run was then normalized to the Montreal Neurological Institute template (MNI152) using an in-house algorithm [31], and combined together using a fixed effects analysis. Within group average across participants was achieved using a mixed effects linear model with fixed effects standard deviations taken from the previous analysis. A random effects analysis was performed by first estimating the ratio of the random effects variance to the fixed effects variance, then regularizing this ratio by spatial smoothing with a Gaussian filter. The variance of the effect was then estimated by the smoothed ratio multiplied by the fixed effects variance. The amount of smoothing was chosen to achieve 100 effective degrees of freedom. The resulting T statistic images were thresholded using the minimum given by a Bonferroni correction and random field theory to correct for multiple comparisons, taking into account the non-isotropic spatial correlation of the errors [32]. To address differences in brain activity between

pre- and post- CN_NINM training with PoNS, a group subtraction analysis was carried out on the data for the group average analysis, using a fixed effects model.