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Response to Letter from Shin and Lee, entitled “FDDNP PET patterns in nondemented populations”

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We appreciate the comments of Dr. Shin and Dr. Lee in response to our recent report describing potential high-risk imaging cluster patterns in FDDNP binding (1), and we wish to clarify that our group's experience with FDDNP imaging is consistent with the important results from Dr. Shin's group pointing to medial temporal FDDNP binding as a potential marker for high-risk subgroups of non-demented individuals (2). In previous analyses of a similar subject group, we found that individuals with mild cognitive impairment who were apolipoprotein E-4 carriers had higher medial temporal binding than non-carriers (3). These results suggest that combining genetic risk measures and medial temporal FDDNP binding values in non-demented individuals could be a useful tool for predicting subsequent neurodegenerative decline.

In our current study (1), we approached the analysis differently: instead of grouping according to diagnosis, we used a cluster analysis, which identified three different subgroups of subjects, according to variations in FDDNP signal patterns. In fact, the medial temporal region distinguished the low FDDNP subgroup from the two higher FDDNP subgroups (Figure 1) and was elevated in both of the higher FDDNP subgroups, which differed from each other according to FDDNP signal patterns in other cortical regions. Thus, the overall findings are consistent with the hypothesis that medial temporal FDDNP binding values are important for distinguishing high from low risk subjects. Moreover, our initial analyses of two-year longitudinal follow-up of 24 non-demented subjects with mild memory complaints (mean [SD] age = 67.7 [9.9] years) indicate that higher medial temporal FDDNP binding values do predict cognitive decline, including verbal memory (Buschke-Fuld total, $t(21) = -2.20$, $p = .04$) and executive function ability (Stroop Interference $t(21) = 2.36$, $p = .03$). Neuropathological studies (4,5) indicating early neurofibrillary tangle accumulation in the medial temporal region in presymptomatic, non-demented individuals, as well as the observation that tangle load, but not plaque load, is associated with cognitive decline in elderly persons, further support the argument from Dr. Shin's group and our group that medial temporal FDDNP binding will eventually demonstrate an advantage in identifying a preclinical stage of Alzheimer's disease.

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