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Dear Editor:

The following is a Letter to the Editor in response to the recent article by Serber et al. (2008) titled "Cognitive test performance and brain pathology." *Nursing Research*, *57*:75-83.

Serber et al. (2008) recently reported significant associations between performance on various "paper and pencil" cognitive measures, including a clock-drawing test (CDT), and regional central nervous system structural changes by magnetic resonance imaging (MRI).

While CDT are often conceptualized as "executive" measures, the truth is actually more complex. Individual CDT vary widely in their psychometric properties as a function of their administration and scoring rubrics (Royall et al., 1999). We have developed a CDT (CLOX) that attempts to distinguish visuospatial function (CLOX2) from its executive control (CLOX1) (Royall, Cordes & Polk, 1998). Watson's CDT may map somewhere between these two extremes, as evidenced by the regions of interest (ROI) whose structure is associated with performance on that task, including the both the right ventromedial frontal cortex, right posterior parietal lobe, and the right posterior temporal cortex.

However, the most interesting finding was that poor CDT performance was also associated with lesions to the posterior insula. The insular cortex modulates autonomic responses to higher emotional and cognitive states. CLOX2 (but not CLOX1) scores have been associated with an increased mortality risk in elderly samples (Lavery et al., 2005; Royall et al., 2007) and may mediate the effect of depressive symptoms on survival (Royall et al., in press). We have hypothesized that these effects are mediated via insular structural lesions, including preclinical Alzheimer's disease (Royall, Gao & Kellogg, 2006).

Insular autonomic control is lateralized in humans. The right insula modulates sympathetic responses, while the left insula modulates parasympathetic responses. Left insular stroke increases mortality in patients with cardiac disease, presumably because it shifts autonomic tone towards excess sympathetic drive, increased heart rate, increased cardiac work-load, lengthened QT intervals, and /or increased afterload (Oppenheimer, Kedem & Martin, 1996). Conversely, right insular lesions may shift the balance towards increased parasympathetic modulation, bradyarrhythmias, syncope and falls.

We have hypothesized that CDT may be vicariously sensitive to right insular brain disease because of the spatial co-localization of the insula with white matter tracts that

convey visuospatial information to the frontal lobes (Royall, Gao & Kellogg, 2006). This may explain why the cognitive correlates of survival are limited to visuospatial tasks, and not executive, language or other cognitive domains (Royall et al., 2007; Antonelli-Incalzi et al., 2006; Royall, 2006). Serber et al.'s finding more directly implicates the insula in CDT performance, supporting our speculation that CDT performance may be useful as a convenient screening tool for fall and cardiac related mortality in a variety of conditions.

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