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## Interventions Transformed through Technology to Improve Cognitive Function in Heart Failure

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Cognitive function is essential to well-being and survival. Among patients with heart failure (HF), cognitive dysfunction was an independent predictor of 12-month all-cause mortality.<sup>1</sup> The cognitive domains most often impaired in HF are memory, attention, working memory, processing speed, and executive function.<sup>2–7</sup> In past studies, 23% to 50% of patients had memory dysfunction<sup>2,3</sup> and 15% to 27% had attention dysfunction.<sup>4,5</sup> Memory and attention are foundational cognitive processes that support the other cognitive functions (e.g., executive function).<sup>8</sup> The most likely etiologies of cognitive dysfunction in HF are cerebral hypoperfusion<sup>9</sup> resulting from decreased cardiac output and cerebral microemboli.<sup>10</sup> Alterations in brain structure and functional connectivity have been identified in the hippocampus and frontal and prefrontal cortex among patients with HF<sup>11,12</sup> and these alterations are consistent with the cognitive domains impaired.

The prevalence of cognitive dysfunction in HF and its association with higher mortality support the urgent need for development and testing of novel interventions that are designed to improve cognitive function and slow cognitive decline. The ideal intervention would meet the following 5 criteria: 1) guided by scientific principles; 2) targeted to specific cognitive domains; 3) tailored to individual cognitive performance levels; 4) deliverable in the home setting to minimize patient and family caregiver burden; and 5) scalable at relatively low cost for delivery to large numbers of patients. Computerized cognitive training and natural restorative environment intervention are guided by scientific principles and have been transformed through technology over time to meet the remaining four criteria. The interventions are being tested for efficacy among patients with HF.

Computerized cognitive training is hypothesized to increase brain plasticity<sup>13,14</sup> and was efficacious in improving memory and working memory among healthy older adults<sup>15,16</sup> and adults with mild cognitive impairment.<sup>17</sup> The computerized cognitive training BrainHQ program, developed by PositScience, is based on scientific principles of plasticity<sup>13,14</sup> and is delivered by computer. The BrainHQ exercises are targeted at specific cognitive domains

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(e.g., memory, working memory), tailored to individual performance, and delivered in the home setting. We found preliminary efficacy of BrainHQ on improved memory<sup>18</sup> and working memory<sup>19</sup> and increased levels of serum brain-derived neurotrophic factor (BDNF), <sup>19</sup> a neurotrophin associated with neuronal plasticity, over 12 weeks among two small samples of patients with HF. Three other studies reported preliminary efficacy of computerized cognitive training using BrainHQ among small samples of patients with HF. <sup>20,21</sup> We are now conducting a randomized controlled trial to test efficacy of BrainHQ to improve the co-primary outcomes of memory and serum BDNF levels and secondary outcomes of working memory, processing speed, instrumental activities of daily living, health-related quality of life, and cost-effectiveness over 8 months (R01 NR016116; ).<sup>22</sup> If efficacious, the home-based computerized cognitive training intervention could easily be delivered to many patients with HF to improve cognitive function.

In Attention Restoration Theory<sup>23,24</sup> Kaplan posited that attention can be restored by interacting with the natural restorative environment and specifically, by immersing oneself in nature (e.g., walking in parks, hiking on nature trails). Empirical evidence has supported this premise among healthy individuals<sup>25,26</sup> and women undergoing treatment for breast cancer. <sup>27</sup> However, patients with HF may be unable to navigate the natural environment because of symptoms of dyspnea and fatigue and adverse factors such as uneven walking surfaces and inclement weather. In a randomized crossover pilot study conducted to test the efficacy of the natural restorative environment to improve attention, Jung and colleagues<sup>4</sup> compared pictures of the nature and built urban environments delivered by laptop computer among patients with HF and healthy control participants and found that participants in both groups had improved attention after viewing the nature pictures. The nature and built urban environment interventions are now being transformed into immersive virtual reality simulations for testing in larger studies to evaluate their efficacy for improving attention in HF (AHA Grant No.19CDA34520006). A prototype of the nature virtual reality simulation has been evaluated for feasibility among 10 patients with HF and was acceptable to patients and usable in the home setting.<sup>28</sup>

A major advantage of interventions transformed by technology is that treatment fidelity can be strengthened by better monitoring and evaluating of the intervention delivery. For example, in BrainHQ the daily time spent performing the intervention and progress completing the program (e.g., errors, correct responses) is captured by the program. However, patients with serious chronic conditions such as HF may have challenges performing the interventions because of troublesome symptoms and lack of experience using the specific technologies. To address these challenges, we developed a nurse-enhanced intervention to be delivered in combination with computerized cognitive training.<sup>18,22</sup> The nurse-enhanced intervention was based on empirical literature about HF-related symptoms, <sup>29</sup> efficacious nurse-led interventions that improved health outcomes among patients with HF,<sup>30–32</sup> and the need for education with support when delivering interventions to persons with serious cardiovascular conditions.<sup>33</sup> In preliminary studies, we found that the nurseenhanced intervention enabled patients to perform and successfully complete the computerized cognitive training.<sup>18,19</sup> Determining the core elements, the amount of intervention needed, and the unique and interactive effects of the nurse-enhanced intervention component is a key area for future research.

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Interventions being transformed by technology offer the promise of better cognitive health for patients with HF. As developing and rigorous testing of these types of interventions continue, further studies are needed in five areas. First, the efficacy of these interventions needs thorough investigation on other neuropsychological (e.g., executive functioning), behavioral (e.g., self-care skills, adherence to medication and physical activity regimens), and health (e.g., mortality, hospital admission) outcomes. Second, biomarkers need to be investigated that are associated with training response and change in outcomes. This information will be essential for future use in practice settings to assist clinicians in determining interventions needs to be determined. Fourth, the amount of time that patients need to spend performing the intervention to derive the most benefit needs to be determined. Finally, an important and broader question deserving of study is whether these interventions can be delivered earlier in the trajectory of serious chronic cardiovascular conditions such as hypertension or acute coronary syndrome to prevent or delay the onset of cognitive dysfunction and HF.

In summary, interventions to improve cognitive function among patients with HF are being transformed by technology. Efficacy testing is ongoing of promising innovative interventions. Nurse enhancement may be essential to facilitate patients' ability to use these interventions over sustained periods of time. The next decade of cardiovascular nursing research will likely yield promising answers about the efficacy and effectiveness of technology-transformed interventions to prevent or delay cognitive dysfunction and improve cognitive health among these vulnerable patients.

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