Plasma cytokine concentrations associated with HIV/hepatitis C coinfection are related to attention, executive and psychomotor functioning

Ronald A. Cohen a,⁎, Suzanne de la Monte a, Assawin Gongvatana a, Hernando Omba c, Beverly Gonzalez c, Kathryn N. Devlin a, Bradford Navia b, Karen T. Tashima a
a Departments of Psychiatry and Human Behavior and Medicine and the Centers for AIDS Research, Brown University School of Medicine, Providence, RI, USA
b Department of Neurology, Tufts University School of Medicine, Boston, MA, USA
c Biostatistics Graduate Program, Brown University School of Medicine, Providence, RI, USA

1. Introduction

HIV-associated neurocognitive and behavioral disturbances are well recognized and continue to occur despite widespread use of highly active antiretroviral therapies (HAART), which can very effectively reduce HIV RNA level and enhances the host immune status. HIV crosses the blood brain barrier and enters the brain very soon after initial infection and replicates in perivascular macrophages and microglia (Budka, 1991). In this regard, HIV infection triggers inflammatory responses associated with microglial cell activation and attendant release of neurotoxic pro-inflammatory cytokines (Gonzalez-Scarano and Martin-Garcia, 2005; Gisolf et al., 2000; Rostasy et al., 2000). The inflammatory component of HIV infection in the central nervous system (CNS) is regarded as a critical component of HIV-associated brain dysfunction (Merrill and Chen, 1991; Cartier et al., 2005; Minagar et al., 2002; Gorg et al., 2006; Guyon et al., 2008; Lewis et al., 2008), with its severity strongly correlating with the abundance of activated monocytes in the brain (Langford and Masliah, 2001). HIV-associated neuronal loss and dysfunction are mediated by increased apoptosis and axonal degeneration throughout the brain (Chiodi, 2006; Sabri et al., 2003; Gray et al., 1996). Frontal-striatal areas have been implicated (Ernst and Chang, 2004; Cloak et al., 2004; Chang et al., 2008; Thompson et al., 2001, 2003; Filippi et al., 2001), consistent with findings of attention-executive and psychomotor impairments common in HIV-infected persons. Neuroimaging approaches, such as magnetic resonance spectroscopy (MRS), can detect abnormalities that reflect cerebral inflammation in HIV-infected people (Chang et al., 2004; Paul et al., 2007, 2008). Previous MRS studies in HIV have shown abnormal cerebral metabolites preferentially in the