Similar impairment has been demonstrated for baseline, but not further evidence is required, therefore these patients may be causative for cognitive deficits in HCV-infected patients. These findings may particularly benefit from HCV eradication. To date, studies addressing the issue of reversibility of cognitive deficits after HCV therapy are based on interferon treatment, which itself can cause continuing cognitive impairment. The important question whether these deficits are indeed reversible after HCV eradication remains unsolved to date.

**Methods.** We conducted an open observational trial with HCV and HCV/HIV coinfected patients and planned HCV treatment. Patients with liver cirrhosis (defined as fibroscan >12.5 kPa), a history of substance dependence, or cerebral diseases were excluded. HIV-infected patients had to have undetectable plasma HIV levels for at least 6 months. We assessed a comparison group of healthy controls (n = 30) for baseline, but not for follow-up. The neuropsychological test battery sufficiently to prevent significant CNS transmigration of lymphocytes 3,6; (2) ongoing steroid treatment of CNS inflammation; (3) effective endogenous remyelination mechanisms in this patient (suggested by complete and timely recovery from previous disabling relapses); and (4) early resolution of encephalopathy enabling effective therapy and accelerated recovery.

The decision to suspend or continue natalizumab in pregnancy must consider risks to both fetus and mother. Although the risks to the fetus of natalizumab exposure appear low and reversible, further evidence is required, particularly long-term data on children exposed in utero. Careful counselling at the time of natalizumab initiation in women of childbearing age is imperative.

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**EFFECT OF INTERFERON-FREE THERAPY ON COGNITION IN HCV AND HCV/HIV INFECTION: A PILOT STUDY**

**OPEN**

Approval of direct-acting antivirals against the hepatitis C virus (HCV) has dramatically changed the management of HCV infection due to high cure rates and a favorable safety profile. Their influence on neurologic aspects is notably relevant, as studies demonstrated active HCV replication within the CNS 1–3 and alterations in cerebral metabolism consistent with neuroinflammatory conditions.2 These findings may be causative for cognitive deficits in HCV-infected patients.3 Similar impairment has been demonstrated in patients coinfected with HIV, with a prevalence as high as 60%.4 Therefore, these patients may particularly benefit from HCV eradication. To date, studies addressing the issue of reversibility of cognitive deficits after HCV therapy are based on interferon treatment, which itself can cause continuing cognitive impairment.1 The important question whether these deficits are indeed reversible after HCV eradication remains unsolved to date.

**Methods.** We conducted an open observational trial with HCV and HCV/HIV coinfected patients and planned HCV treatment. Patients with liver cirrhosis (defined as fibroscan >12.5 kPa), a history of substance dependence, or cerebral diseases were excluded. HIV-infected patients had to have undetectable plasma HIV levels for at least 6 months. We assessed a comparison group of healthy controls (n = 30) for baseline, but not for follow-up. The neuropsychological test battery...
Table Cognitive performance at baseline before therapy

| Domains evaluated      | Infected (n = 25) | Control (n = 30) | p Value |
|------------------------|-------------------|-----------------|---------|
| Visual learning/memory |                   |                 |         |
| Rey-Osterrieth Complex Figure: immediate recall | 51.73 (11.48) | 62.68 (11.00) | 0.001   |
| Rey-Osterrieth Complex Figure: delayed recall | 50.50 (10.82) | 62.00 (10.81) | 0.000   |
| Attention/working memory |                |                 |         |
| Digit span: forwards   | 50.71 (12.04)    | 59.88 (7.84)    | 0.002   |
| Digit span: backwards  | 49.63 (11.00)    | 61.13 (8.66)    | 0.000   |
| d2 Test of attention: concentration | 43.24 (8.33) | 51.50 (8.60) | 0.001   |
| Executive function     |                   |                 |         |
| Color-Word Interference Test | 47.60 (11.00) | 54.83 (7.69) | 0.012   |
| Trail-Making Test Part B | 49.22 (12.69) | 57.33 (7.63) | 0.005   |
| Processing speed       |                   |                 |         |
| Trail-Making Test Part A | 48.35 (10.50) | 55.20 (8.04) | 0.008   |

Values are presented as mean (SD) of t scores for all tests.
* Not significant: language/verbal fluency, logical thinking/nonverbal intelligence level.

At follow-up assessment, patients did not show cognitive decline in any domains compared to baseline; neither did any patient report subjective impairment during or after the therapy. On the contrary, 2-tailed t tests indicate a significant ($p < 0.05$) improvement in the domains visual memory, processing speed, attention, and executive functioning. In addition, we observed a significant ($p = 0.022$) decline in self-reported fatigue severity. There was no significant change in the level of depression, but an increase in self-reported quality of life.

Discussion. In this study, we investigate the effect of an interferon-free treatment on cognitive function in HCV-monoinfected and HCV/HIV coinfected patients. Our data show that HCV-infected patients without comorbidities had significantly poorer cognitive performance than controls. Against our expectations, HIV coinfection did not increase the extent of cognitive deficits. These findings partially contradict conclusions made by other studies. A recent study showed that HCV coinfection did not have an effect on cognitive function in a cohort of HIV-infected patients, which led the authors to question an influence of HCV on cognition per se.

In contrast, our data suggest a significant influence of HCV infection on cognitive function, which seems to outweigh that caused by HIV infection. Our first follow-up data support this assumption, showing an improvement in those cognitive domains that were impaired before HCV eradication. Our study was explicitly designed to detect differences attributable to HCV eradication. In contrast to the cross-sectional approach of most previous studies, we therefore chose a longitudinal approach.

Nevertheless, these first data have to be interpreted carefully due to small sample size. Practice effects might partially contribute to the observed improvements. However, reported effect sizes are relatively small (Cohen $d = 0.00$–0.24) compared to the ones seen in our cohort ($d = 0.20$–1.79). To verify an improvement, more follow-up data need to be considered using a reliable change index approach to differentiate between practice effects and treatment-related cognitive changes.

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