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To the Editors:
We read with great interest the article by Nielen & Den Boer (**33**, 917–925), who found that patients with obsessive–compulsive disorder (OCD) displayed cognitive deficits consistent with a dysfunction of the dorsolateral-striatal circuit (DLSC) (i.e. impairments in planning ability, spatial memory, and motor speed). According to the report, the 'successful' treatment of patients with OCD with fluoxetine did not alter cognitive functions 'to any significant degree'. The authors argued that cognitive impairments in OCD may form a trait-feature of the disorder and that fluoxetine produces its clinical effects by acting on a neural system whose cognitive functions were not measured in their study (presumably those subserved by the orbitofrontal-striatal circuit).

There are, however, a certain number of empirical findings that apparently challenge the authors' conclusions regarding the relatively minor role played by the DLSC in the treatment of OCD with selective serotonin reuptake inhibitors (SSRIs). Hollander & Wong (1996) found that impairment in cognitive functions presumably subserved by the DLSC (Trail Making Test B–A) are associated with a blunted prolactin response to m-CPP (a probe for serotonergic function) in patients with OCD. A recent study reported that cognitive deficits that are suggestive of a dysfunction in the DLSC (verbal fluency-letters) in patients with OCD may be state-related and, therefore, more amenable to treatment (Kim *et al*. 2002). Abbruzzese *et al*. (1995) found that patients with OCD treated with fluvoxamine exhibited a better performance in the WCST (a test thought to tap the DLSC) as compared to their unmedicated counterparts. Finally, at least one study (Fontenelle *et al*. 2001) observed that a poorer performance in the WCST in patients with OCD was associated with a better therapeutic response to SSRIs.

In our opinion, it would be counterintuitive to expect that patients with OCD who have not responded to treatment with fluoxetine (44% of the total) would exhibit significant improvements in their neuropsychological performance. Instead of investigating the OCD group as a whole (responders and non-responders), it would be interesting if Nielen & Den Boer could focus their analysis on the treatment responders group. Did this group of patients displayed improvements in their cognitive function, while the treatment non-responders did not? We believe that this kind of analysis might provide us with additional relevant findings. Maybe the authors can take a second look at their data with this perspective.

REFERENCES

Abbruzzese, M., Ferri, S. & Scarone, S. (1995). Wisconsin Card Sorting Test performance in obsessive–compulsive disorder: no evidence for involvement of dorsolateral prefrontal cortex. *Psychiatry Research* **58**, 37–43.

Fontenelle, L., Marques, C., Engelhardt, E. & Versiani, M. (2001). Impaired set-shifting ability and therapeutic response in obsessive–compulsive disorder. *Journal of Neuropsychiatry and Clinical Neurosciences* **13**, 508–510.

Hollander, E. & Wong, C. M. (1996). The relationship between executive function impairment and serotonergic sensitivity in obsessive–compulsive disorder. *Neuropsychiatry Neuropsychology and Behavioral Neurology* **9**, 230–233.

Kim, M. S., Park, S. J., Shin, M. S. & Kwon, J. S. (2002). Neuropsychological profile in patients with obsessive-compulsive disorder over a period of 4-month treatment. *Journal of Psychiatric Research* **36**, 257–265.

Nielen, M. M. A. & Den Boer, J. A. (2003). Neuropsychological performance of OCD patients before and after treatment with fluoxetine: evidence for persistent cognitive deficits. *Psychological Medicine* **33**, 917–925.

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The Authors reply:
Fontenelle, Mendlowicz and Versiani make a plausible case for the necessity to analyse not

only the OCD group as a whole, but also to compare responders and non-responders to treatment in a separate analysis. In view of their comments we have taken up their suggestion to reanalyse our data. As described in the original paper (Nielen & Den Boer, 2003), responders ($N=12$) were defined as patients with a minimum reduction of 40% on the total score on the Y-BOCS.

Performance on the four executive tasks (SWMT, TOL, IDED and Stroop) was reanalysed with repeated measures ANOVA using session as the within-subject factor. With respect to the between-subject factor 'group', we compared performance of responders and non-responders. In case of significant differences between these OCD subgroups, we subsequently tested whether responders differed from the normal controls. For measures on the SWMT (total between-errors and strategy score), TOL accuracy (number of perfectly solved solutions and total number of excess moves), TOL latency, and ID-EDS (number of trials on ID and ED stage) there were no significant group × session interactions or main effects. Only for the Stroop task (level of interference) we found a main effect of group, indicating that non-responders were in general more susceptible to interference ($F_{1,16}=5{\cdot}56$, $P=0{\cdot}031$) than responders. When we subsequently compared performance of responders with that of normal controls, there was a significant group × session interaction ($F_{1,16}=5{\cdot}93$, $P=0{\cdot}020$). However, this just seems to replicate the subtle interaction effect that was already present in the whole OCD sample. In other words, reanalysing the data by comparing performance of responders and non-responders, and responders with normal controls did not essentially alter the findings we already observed in the entire OCD sample.

In their critique, Fontanelle and colleagues propose that the DLPFC plays a more important role than is suggested by our findings. They argue that there are several empirical studies supporting an association between DLPFC function and treatment response in OCD. However, we are not quite sure whether the findings of these studies unequivocally demonstrate a direct relationship between DLPFC function and therapeutic response to a SSRI. First, except from our own report, it was only Kim *et al*. (2002) who directly investigated the effect of pharmacological treatment on neuropsychological performance. In their study, there was an effect of treatment on the COWA-letter task, however, it should be added that this task does not seem to be a very specific marker of DLPFC function. For instance, COWA-letter fluency has been reported to recruit medial and orbital prefrontal regions as well (Phelps *et al*. 1997; Kim *et al*. 2002; Ravnkilde *et al*. 2002). In addition, directly manipulating activity in the central serotonergic system of remitted depressive patients has been shown to affect neural activity elicited by verbal fluency tasks (Smith *et al*. 1999). Serotonin is increasingly associated with the functions of medial and orbital PFC, and not DLPFC (Robbins, 2000), so this makes it less likely that verbal fluency is exclusively linked to the DLPFC.

In their own study, Fontenelle and colleagues investigated the relationship between treatment and performance on tasks for the DLPFC rather indirectly. That is, Fontenelle *et al*. (2001) associated baseline WCST performance to treatment outcome but it was not quite clear whether the two groups of responders and non-responders were carefully matched before they entered treatment. For instance, performance on the WCST is significantly influenced by factors such as education or the presence of depressive symptoms (Gambini *et al*. 1992; Beats *et al*. 1996). Unfortunately, Fontenelle *et al*. (2001) do not report whether responders displayed comparable levels of education or depressive symptoms as non-responders. In our opinion, this hampers firm conclusions about the significance of the reduced WCST performance in OCD responders.

Taken together, we believe that there is as yet no strong evidence in the literature for a prominent role of the DLPFC in the treatment of OCD. This conclusion is supported by our own data showing no differential performance of responders and non-responders on tasks for DLPFC function.

REFERENCES

Beats, B. C., Sahakian, B. J. & Levy, R. (1996). Cognitive performance in tests sensitive to frontal lobe dysfunction in the elderly depressed. *Psychological Medicine* **26**, 591–603.

Fontenelle, L., Marques, C., Engelhardt, E. & Versiani, M. (2001). Impaired set-shifting ability and therapeutic response in obsessive–compulsive disorder. *Journal of Neuropsychiatry and Clinical Neurosciences* **13**, 508–510.

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Gambini, O., Macciardi, F., Abbruzzese, M. & Scarone, S. (1992). Influence of education on WCST performances in schizophrenic patients. *International Journal of Neuroscience* **67**, 105–109.

Kim, M. S., Park, S. J., Shin, M. S. & Kwon, J. S. (2002). Neuropsychological profile in patients with obsessive–compulsive disorder over a period of 4-month treatment. *Journal of Psychiatric Research* **36**, 257–265.

Nielen, M. M. A. & Den Boer, J. A. (2003). Neuropsychological performance of OCD patients before and after treatment with fluoxetine: evidence for persistent cognitive deficits. *Psychological Medicine* **33**, 917–925.

Phelps, E. A., Hyder, F., Blamire, A. M. & Shulman, R. G. (1997). FMRI of the prefrontal cortex during overt verbal fluency. *Neuroreport* **8**, 561–565.

Ravnkilde, B., Videbech, P., Rosenberg, R., Gjedde, A. & Gade, A. (2002). Putative tests of frontal lobe function: a PET-study of brain activation during Stroop's Test and verbal fluency. *Journal Clinical and Experimental Neuropsychology* **24**, 534–547.

Robbins, T. W. (2000). From arousal to cognition: the integrative position of the prefrontal cortex. *Progress in Brain Research* **126**, 469–483.

Smith, K. A., Morris, J. S., Friston, K. J., Cowen, P. J. & Dolan, R. J. (1999). Brain mechanisms associated with depressive relapse and associated cognitive impairment following acute tryptophan depletion. *British Journal of Psychiatry* **174**, 525–529.

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