implications for future differential diagnoses of first-onset psychosis, potentially involving relevant auto-antibody and, specifically, anti-NMDA receptor screening. Further, plasmapheresis may be required and in some cases may even be clinically indicated before a diagnosis of NMDA receptor encephalitis is confirmed. This will have implications for hospital resources and will require close liaison between psychiatry and neurology services.

N-methyl-D-aspartate receptor hypofunction, whether due to exposure to phencyclidine ingestion, NMDA receptor auto-antibody or altered NMDA receptor trafficking,[7,8] is now implicated even more strongly in schizophrenia. Future studies focusing on this area may provide clues not only to the screening and management of NMDA receptor encephalitis among first-episode psychosis populations, but may also lead to a broader understanding of schizophrenia pathophysiology, with the potential for development of novel treatment strategies.

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Occipital transcranial magnetic stimulation in dementia with Lewy bodies

The results of Taylor *et al*'s study[1] are intriguing, shedding light on the pathogenesis of visual hallucinations in dementia with Lewy bodies.

However, I have some concerns about its methodology. The authors did not adopt the rather restrictive (and currently used) definition of phosphene threshold (i.e. the lowest stimulus intensity required to elicit phosphenes in 50% of trials), but used a much lower value (25%) to minimise the number of participants who might not respond. Moreover, to ensure inclusion of all individuals in analyses, participants who did not report phosphenes up to 100% stimulator output were arbitrated a phosphene threshold of 101%. The authors therefore assumed that not reporting phosphenes meant having a threshold above 100% because of an insufficient magnetic field strength from the stimulator to induce phosphenes in these individuals. However, as far as I know, to date there is no evidence definitely demonstrating such an assumption.

As a matter of fact, in most published studies of phosphene thresholds a certain number of participants do not experience phosphenes even with a maximum stimulator output. There are some reasons which may (partially) explain such a phenomenon.

First, it is possible that owing to methodological difficulties in mapping phosphene thresholds over each square millimetre of the occipital skull, the correct point for stimulation may not be identified in each participant.

Second, unlike primary motor cortex, primary visual cortex (calcarine fissure) is deeply located, lying in the mid-sagittal plane, so that the magnetic field strength applied over the entire skull may be insufficient to reach and stimulate the visual cortex. Regarding this aspect, it is noteworthy to consider that Taylor *et al* used a figure-of-eight coil (and not a circular one), which, although it is much more selective and has a higher spatial accuracy, stimulates a smaller cortical area,[2,3] and may generate, at least theoretically, a weaker electric current, resulting in a lower probability of evoking phosphenes.

Finally, as the authors stated, every millimetre the surface cortex is away from the stimulating coil, approximately an additional 3% of the maximum power output is required to induce an equivalent level of brain stimulation at the motor cortex (although no similar data on visual cortex stimulation are available in the literature). Such an aspect needs to be taken into account not only with regard to occipital cortical atrophy in affected patients compared with healthy controls, but also with regard to the fact that, because the lower portion of the visual cortex representing the upper visual field is farther from the scalp (as observed in magnetic resonance imaging), it is more difficult to elicit phosphenes with transcranial magnetic stimulation in the upper than in the lower visual field.[4] Although in the study an adjusted phosphene threshold ratio was performed to account for possible group differences in atrophy, it is not clear whether other aspects (anatomical differences in skull thickness and portion of visual cortex stimulated) were considered.

In the light of the above, I think that the authors should have performed a statistical analysis of phosphene threshold including only those participants in whom phosphenes were actually induced.

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Authors' reply: We agree that phosphene thresholds are typically defined at the 50% response rate level, although it should be recognised that the setting of a threshold is an arbitrary process. A number of our participants had thresholds near and

approaching the maximum stimulator output and use of a lower level of threshold acceptance allowed for a more precise estimation of their visual cortical excitability. Importantly, given the comparability between stimulus response plots of controls and patients with dementia with Lewy bodies (Fig. 2),[1] it is unlikely that use of a 25% cut-off for threshold adversely affected our findings.

Dr Brigo highlights the issue of non-response to the stimulation and that this may be as a result of causes other than insufficient stimulation strength. Indeed, phosphene perception, or lack of, may not necessarily originate in the visual cortex but may depend on higher visual areas or indeed non-visual areas as well as recurrent processing.[2,3] However, the reasons that Dr Brigo presents to explain the non-response – including imprecision in finding the optimal position for stimulation delivery over the occiput, greater depth of the primary visual cortex leading to reduced magnetic field strength at the level of the cortex, and use of the figure-of-eight coil – are actually arguments supporting the assumption that failure to respond in some individuals is due to insufficient current stimulation to the neural locus responsible for phosphene elicitation.

In our study we sampled nine equally spaced scalp sites, giving good symmetrical cover of the occiput; this was a compromise between precision and limiting the experiment duration in a vulnerable patient group. The figure-of-eight coil has been frequently used in phosphene research (e.g. Kammer *et al*[4]) and was chosen because of its spatial accuracy; larger, diffuse-field coils could theoretically activate areas external to the visual areas of interest or indeed induce retinal phosphenes. In addition, we would contend that the transcranial magnetic stimulation (TMS) methodologies we employed meant that we had comparable and, in some cases, better rates of phosphene response compared with other studies in young healthy individuals.

Dr Brigo indicates potential differences in the lower and upper visual cortical activation with TMS and certainly our data of greater phosphene elicitation in the lower visual fields supports this. Our use of the adjusted phosphene threshold ratio to control for group differences in atrophy also accounted for skull thickness, although whether the positions we chose for these measurements directly related to the precise locus of stimulation on the visual cortex, we agree, is a methodological limitation. The use of magnetic resonance-guided stereotactic coil placement, for example, would help with this issue and allow for more precise threshold determination.

As suggested by Dr Brigo we performed an analysis only on those participants who responded to TMS (controls, $n=17$; patients, $n=17$) and the findings were in line with our main analyses: there were no significant differences between the controls and patients for phosphene threshold (controls: median 64.0% (IQR = 32.5%); patients: median 67.0% (IQR = 20.0%); $U=139.5$, $P=0.87$) and phosphene response rate (controls: median 6.0 (IQR = 7.0); patients: median 8 (IQR = 5); $U=112.5$, $P=0.27$). Correlations between the Neuropsychiatric Inventory hallucinations subscale score in patient responders and the phosphene excitability measures (phosphene threshold, Kendall's $t=-0.28$, $P=0.15$; phosphene response rate, $t=0.46$, $P=0.02$) were in the same direction as the main analysis, although less significant owing to the smaller sample and the fact that the four patients who did not respond to TMS at the maximum stimulator output had significantly less severe and frequent visual hallucinations compared with patient responders (Mann–Whitney U-test 16.5, $P<0.001$). Clearly, the lack of phosphene response (regardless of cause) is associated with fewer visual hallucinations and thus we would argue that inclusion of non-responders in our analyses is essential in providing a more holistic understanding of the underlying aetiology of this symptom in dementia with Lewy bodies.

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Creativity and mental disorder

Kyaga *et al* found an intriguing association between creativity and severe mental disorder.[1] The study draws its strength from a large sample size. However, the retrospective data collection methodology brings with it certain inherent limitations, which the authors have acknowledged, and causal links have been hinted at in the discussion. We would like to bring to attention two issues. First, the role of potential confounders in selection of occupation has not been taken into consideration. The type of occupation one pursues is governed by multiple factors in addition to personnel interest, including educational qualification, opportunity, awareness, location of the job, financial remuneration, familial and other social commitments.[2] Many of these variables are likely to be affected by the psychiatric illness, although they are modifiable by many independent factors as well. Hence the occupation choices of both individuals with mental illness and their children (and other family members) are likely to be affected by many variables which need to be taken into consideration when interpreting Kyaga *et al*'s findings.

Another relevant issue for consideration is the way occupation is defined in their study. The definition of occupation used in (mental) health studies has been criticised for being too restrictive.[3] National descriptions of occupation tend to classify only those occupations that have economic relevance.[4] Such an approach is likely to miss someone employed as a labourer who paints during their leisure time or to miss certain population groups. For example, in many settings the majority of women are likely to be the primary caregiver (i.e. housewife) and not formally 'employed'. Future studies could be strengthened by the use of a more comprehensive and inclusive definition of occupation.

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