**Correspondence**

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**False-positive results with an alcometer device**

We write to report false-positive results with an alcometer device (Lion S-D2 brand) when it is used in the vicinity of recently applied alcohol disinfectant hand rub.

The Orchard Clinic is a medium secure forensic unit set within the grounds of the Royal Edinburgh Hospital. The use of an alcometer is essential in the treatment of Scottish government ‘restricted’ patients or if there is suspicion or evidence of alcohol misuse. Indeed, all staff receive training on the use of the alcometer during their induction period.

Recently a patient with ‘restricted’ status returned from leave outwith the clinic. On the patient’s return they were breathalysed. The alcometer gave a reading of 0.04 mg/lBrAC – equivalent to just under one unit of alcohol. The patient denied consuming alcohol. Staff had used an alcohol-based hand disinfectant lotion prior to carrying out the test. This was consistent with hand hygiene guidelines following the H1N1 flu pandemic.

We later reproduced the positive alcometer results after using alcohol hand lotion in the standard way. The reading rose from 0.01 mg/lBrAC (background reading) to 0.1 mg/lBrAC – equivalent to two units of alcohol.

The alcohol hand rub used within NHS Lothian is up to 80% alcohol, which is one of the highest on the market.1 It is therefore likely there is much alcohol in the vapour around where it is used. When the individual inhales prior to the test, some alcohol vapour is also taken in which is exhaled back into the instrument as part of their sample.

False-positive alcometer results may have serious implications for the treatment of forensic patients. No other report of alcohol hand lotion raising alcometer readings was found in the literature. It had not been reported as an issue with local colleagues in the Alcohol Problem Service or with Lothian and Borders Police. However, it is recognised that the police may carry out the test in a more open environment than a ward treatment room.

In addition to reporting this finding to the manufacturer, the local procedure for operating the alcometer has now been amended to ensure that alcohol hand lotion: (a) is not used by any staff involved in taking an alcometer reading at least 5 min before taking the test; and (b) is not used in the same room at least 5 min before a test is carried out.

Staff are encouraged to use soap and water to clean their hands before administering an alcometer test.

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**Molecular genetics and the relationship between epilepsy and psychosis**

We read with interest the paper by Adachi et al1 in which they conclude that early development of interictal psychosis in people with epilepsy may reflect individual vulnerabilities to psychosis, including genetic, rather than being driven by epilepsy-related damage.

As they point out, their conclusion challenges traditional assumptions about the relationship between epilepsy and psychosis, many of which have been based on relatively sparse data. It is of interest that recent molecular genetic findings in psychosis suggest that the comorbidity of psychotic symptoms and epilepsy is a product of shared underlying biological mechanisms. For example, specific genomic structural variants (copy number variants) have been described that predispose to schizophrenia, epilepsy, as well as some other ‘neurodevelopmental’ phenotypes such as autism and intellectual disability.2 Individuals with such structural variants do not typically have both schizophrenia and epilepsy, but rather some with a variant have schizophrenia, others have epilepsy, and others have a different phenotype or are unaffected. This means that the relationship cannot be caused simply by ‘toxic’ effects of epileptic seizures on the brain. Rather the finding strongly suggests that one or more genes, the function of which is disturbed by the structural variant, play(s) a role in the pathogenesis of both epilepsy and psychosis.

A second recent observation of potential interest concerns genes encoding ion channels. Ion channelopathies are known to underlie some epilepsies, so it is of great interest that variation within the gene CACNA1C (encoding a subunit of the L-type voltage-dependent calcium channel) is associated with schizophrenia, epilepsy, as well as recurrent depression and bipolar disorder.3,4 This suggests that ion channel dysfunction may also be involved in mood and psychotic illness. Again, this provides support for the possibility that some individuals might experience both psychosis and epilepsy at least in part because of an underlying vulnerability to both.

It is likely that as the understanding of brain function increases we will move closer to understanding the complexities, multiple associations and comorbidities that commonly occur in psychiatric illness. A sufficient number of adequately trained psychiatrists working within appropriate services will be vital for translating this knowledge into benefits for patients.5

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4 Green EK,Grozeva D, Jones I, Jones L, Kirov G, Caesar S, et al. The bipolar disorder risk allele at CACNA1C also confers risk of recurrent major...
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Heterogeneity of coordinate-based meta-analyses of neuroimaging data: an example from studies in OCD

Two automated, coordinate-based meta-analyses of voxel-based morphometry (VBM) studies comparing individuals with obsessive–compulsive disorder (OCD) and healthy controls have been recently published, respectively, in the *British Journal of Psychiatry* and *Neuropsychopharmacology*. Surprisingly, their results are less concordant than one would have expected. We believe this is largely due to methodological differences across the studies.

In coordinate-based meta-analysis, three-dimensional brain maps are built based on the reported coordinates of voxels of peak statistical difference between groups, with higher values being assigned to voxels closer to these coordinates. The full-width at half maximum (FWHM) value of a Gaussian kernel determines the width of spatial distribution, thus critically influencing the results. Radua & Mataix-Cols used a 25 mm FWHM kernel, whereas Rotge et al. set this parameter at 12 mm. Such distinction may explain two differences between their results. First, only Radua & Mataix-Cols reported grey matter increases in the right superior parietal cortex and precuneus, although both studies took exactly the same parietal cortical coordinates (n = 4) from the individual VBM investigations. However, these parietal coordinates were not in close proximity to each other, possibly reflecting the spatial uncertainty of OCD-related abnormalities in this area. Since the width of the distribution of voxel values reflects the spatial uncertainty of significant findings, the greater FWHM kernel used by Radua & Mataix-Cols possibly afforded greater sensitivity to detect parietal clusters of grey matter difference. Second, although both studies detected striatal foci of increased grey matter, Rotge et al.’s findings were confined to the putamen, whereas in the study by Radua & Mataix-Cols these foci spread also to the globus pallidus and caudate nucleus. The greater FWHM value used by Radua & Mataix-Cols probably explains the lower spatial resolution of the striatal foci in their meta-analysis.

Moreover, Rotge et al. used the activation likelihood estimation method, in which coordinates regarding increased and decreased grey matter are separately computed in independent maps. Conversely, Radua & Mataix-Cols used the signed differential mapping method, in which coordinates for findings of either increased or decreased grey matter are reconstructed in the same region of critical relevance to the pathophysiology of OCD. An additional source of discrepancy relates to the criteria for coordinate selection. Rotge et al. included all coordinates reported in the selected studies, regardless of statistical thresholds and correction for multiple comparisons. Conversely, Radua & Mataix-Cols employed stricter criteria, thus leading to the inclusion of fewer coordinates (as detailed in their article).

In conclusion, these papers are an example of how methodological differences may critically influence the results of coordinate-based meta-analyses. Therefore, when performing such investigations, one should clearly justify the criteria used for coordinate selection and the choice of other methodological parameters. Future studies using such novel techniques should focus on how to foster greater methodological comparability and reproducibility of results.

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Authors' reply: As pointed out by Ferreira & Busatto, one parameter critically influencing the results of a coordinate-based meta-analysis is the FWHM of the kernel. The optimal FWHM has been found to depend on the meta-analytic method. In signed differential mapping (SDM), a 25 mm FWHM shows a good compromise between sensitivity and control of false positives. This FWHM may account for different sources of spatial error such as registration mismatch, the size of original clusters or the location of the peak coordinates within the clusters. Much smaller FWHMs are common in activation/anatomical likelihood estimation (ALE), usually 10–15 mm. However, the use of these small FWHMs has not been clearly justified and it might lead to a dramatic reduction in sensitivity. Salimi-Khorshidi et al. found that the sensitivity of the ALE method with a standard deviation of 5 mm (corresponding to 10–15 mm FWHM) was approximately 50% of the sensitivity achieved with a standard deviation of 15 mm (corresponding to 35 mm FWHM).

Other limitations of ALE may be more serious and have motivated the development of other methods such as SDM. For example, coordinates of increased and decreased activation (or, in this case, grey matter volume) are computed separately. This means that when calculating the meta-analytic increase in a voxel, the (negative) values of those studies reporting decreases in the same voxel are artificially replaced by zeros, leading to an inflation of the meta-analytic decrease. Therefore, brain regions with higher variability are more likely to be detected as significant in the meta-analysis, to the extent that some brain regions may appear to have both increases and decreases at the same time (e.g. see Mennies et al. This is both mathematically and physiologically implausible. Another advantage of SDM is the strict inclusion of coordinates that are statistically significant at the whole-brain level and using the same threshold throughout the brain. This is of utmost importance given that it is not uncommon in neuroimaging studies that some regions (e.g. a priori regions of interest) are more liberally thresholded than the rest of the brain, thus potentially leading to false positives.

Unfortunately, psychiatric neuroimaging is plagued with methodological problems such as small sample sizes and overly liberal statistical methods, often making findings hard to replicate. Meta-analytical methods have the potential to overcome some of these limitations by helping researchers ‘see the forest before the trees’. However, if the methods or its parameters are not chosen rigorously, meta-analyses may suffer from the same problems that motivated their development in the first place.


Correction

Association between extreme autistic traits and intellectual disability: insights from a general population twin study. BJP, 195, 531–536. Table 1 (p. 534): the figures in parentheses are upper and lower boundaries (+/−) of the 95% confidence intervals, calculated using corrected standard errors (not s.d. values, as originally reported). The online version of this table has been corrected post-publication in accordance with this correction.

doi: 10.1192/bjp.197.1.77a
Heterogeneity of coordinate-based meta-analyses of neuroimaging data: an example from studies in OCD
Luiz Kobuti Ferreira and Geraldo F. Busatto
BJP 2010, 197:76-77.
Access the most recent version at DOI: 10.1192/bjp.197.1.76 a

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http://bjp.rcpsych.org/ on November 8, 2016
Published by The Royal College of Psychiatrists