When is a conjunction not a conjunction?

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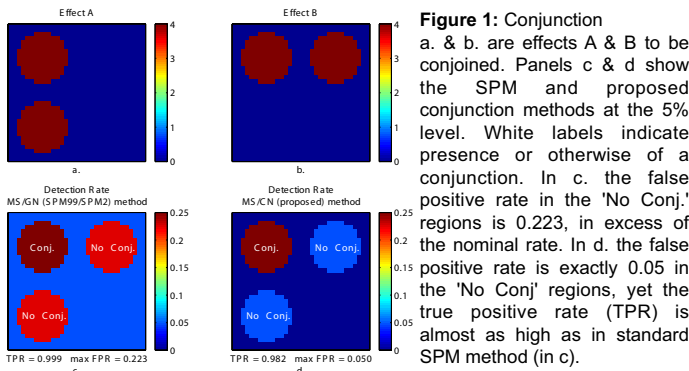
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Summary

Many neuroimaging studies need to look for areas of overlap or conjunction of effects. The most commonly used test for conjunction is the minimum statistic method proposed by Friston *et al* [1] and implemented in SPM. We argue that this method is not a valid test for conjunction in the sense that it is usually understood. We set out the standard definition for a conjunction, and derive a simple and valid alternative method based the minimum statistic.

What is a conjunction?

If we have two truth statements *p* and *q*, then the conjunction of *p* and *q* is true if and only if both *p* AND *q* are true. In neuroimaging terms, the statements *p* and *q* are statements for each voxel about the presence of an effect for a particular comparison. For example, say we have a binary image identifying the areas where an effect of task *A* is truly present; this image contains a 1 in voxels where there is a real effect for task *A* and zeros elsewhere. We have a similar binary image for task *B*. The *conjunction* map of *A* and *B* will contain 1 for voxels where there activation for task *A* AND there is activation for task *B*, with zeros elsewhere. Figure 1 illustrates this definition. Panel a illustrates effect *A*; b shows a map for effect *B*. There is only a conjunction of effects in the circle at the top left.

Figure 1: Conjunction a. & b. are effects A & B to be conjoined. Panels c & d show the SPM and proposed conjunction methods at the 5% level. White labels indicate presence or otherwise of a conjunction. In c. the false positive rate in the 'No Conj.' regions is 0.223, in excess of the nominal rate. In d. the false positive rate is exactly 0.05 in the 'No Conj' regions, yet the true positive rate (TPR) is almost as high as in standard SPM method (in c).

Conjunctions and the null hypothesis

The conjunction null hypothesis is the state of no conjunction of effects. If the conjunction hypothesis is *A* AND *B*, then the conjunction null hypothesis is: (not *A*) OR (not *B*).
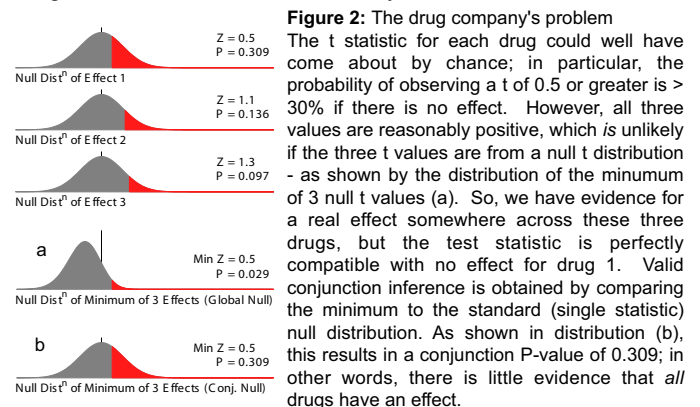
SPM conjunctions using the minimum statistic

Friston *et al* [1] proposed a test for conjunction using the minimum t statistic. Imagine a voxel where the t statistic for *A* and *B* are 0.8 and 1.6. Neither value is convincing on its own, but *both* values are well above zero, which suggests there may be a real effect. This can be formalized by testing the minimum t value. If there is no effect then both t statistics will be drawn from a random (null) t distribution. One can find uncorrected and corrected thresholds for a minimum of two or more t statistics [2]. We compare the observed minimum t value to the null minimum t distribution to see if the observerd value is unlikely by chance. The minimum t from *A* and *B* is 0.8. 0.8 falls in the top 5% of the distribution for the minimum of two null t values, so we conclude that this pair of values was unlikely to have come about by chance. This is the conjunction method implemented in SPM99 and SPM2.

The problem with SPM conjunctions

The SPM conjunction method compares the minimum t statistic to the null distribution of a minimum t statistic. This null distribution assumes there is no effect for *A* and there is no effect for *B*. In general the method tests against the null hypothesis of *no* effect in *any* of the comparisons, so we will call this method Minimum Statistic compared to the **Global Null** (MS/GN). This is not a test for logical AND. The correct null hypothesis for an AND conjunction is that one or more of the comparisons has not activated. The MS/GN test has a different null hypothesis, which is that none of the comparisons have activated. This last null hypothesis can be refuted if any comparison has activated.

Consider the following pharmaceutical parable. Three drug companies have each made a drug which they hope will reduce blood pressure. Each company ran a study comparing their own drug to placebo, giving t values of 0.5, 1.1 and 1.3. None of the individual drugs had a "statistically significant" effect on blood pressure. Then a statistician for the company making the first drug suggested that instead of testing the drugs invidually, they should test if *all* of the drugs had an effect. The MS/GN threshold for the minimum of 3 t values is 0.3361, so the MS/GN test is significant. If the drug company interprets this test as a logical AND, they would think they had hard statistical evidence that their drug was effective, when this is clearly not the case.

Figure 2: The drug company's problem
The t statistic for each drug could well have come about by chance; in particular, the probability of observing a t of 0.5 or greater is > 30% if there is no effect. However, all three values are reasonably positive, which *is* unlikely if the three t values are from a null t distribution - as shown by the distribution of the minumum of 3 null t values (a). So, we have evidence for a real effect somewhere across these three drugs, but the test statistic is perfectly compatible with no effect for drug 1. Valid conjunction inference is obtained by comparing the minimum to the standard (single statistic) null distribution. As shown in distribution (b), this results in a conjunction P-value of 0.309; in other words, there is little evidence that *all* drugs have an effect.

SPM conjunctions are often misinterpreted

We analysed all HBM2003 abstracts that used SPM conjunction analysis. We classified abstracts as **incorrect** if there was evidence that the authors interpreted the MS/GN as a logical AND. Of 42 abstracts using SPM conjunctions, 66% were incorrect.

A valid test for conjunction

A valid test must control the worst-case false positive rate. Usually, a null hypothesis is 'simple', and corresponds to a zero effect, and there is only one "case". The conjunction null hypothesis is 'composite', and is a union of many cases, all of the possible situations where one or more effects is null. The worst-case situation is that of exactly one effect null, and all other effects large [3]. In this situation, the distribution of the minimum statistic is just an individual test statistic (a single t, not a minimum of t's), and hence valid conjunction inference follows from comparing the Minimum Statistic to the usual critical threshold (corrected or uncorrected). This test gives the correct rate of false positives in areas where activation is not common across conditions (see figure 1). The test is valid even if the comparisons are not independent. See poster WE 260 for more detail.

References: [1] Friston et al (1999) NeuroImage 10:385; [2] Worlsey & Friston (2000) Statistics & Probability Letters 47:135. [3] Nichols et al, in preparation: avaliable at http://www.sph.umich.edu/~nichols/Conj