Response to “Mosaic Brains? A Methodological Critique of Joel et al. (2015)”, by Marco Del Guidice, Richard A. Lippa, David A. Puts, Drew H. Bailey, J. Michael Bailey, and David P. Schmitt, an Online document – December 23, 2015

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I am very glad that our PNAS paper (Joel et al., 2015) has raised discussions around the important question of the relations between sex and the brain in general and about our new methodological approach in particular. I think Marco Del Giudice and his colleagues have carried out several very interesting and relevant analyses and simulations, which, as explained below, strongly support our approach and conclusions regarding the brain. I hope we can soon pull outside of the dimorphism-difference formulation and start characterizing the population of human brains and studying the complex interplay between sex and other factors that underlie brain structure, function and dysfunction (Joel & Fausto-Sterling, in press).

The question we were trying to answer in the PNAS paper is how far the categories “male” and “female” extend beyond the genitalia, and in particular, into the human brain. As stated in the Abstract: “Documented sex/gender differences in the brain are often taken as support of a sexually dimorphic view of human brains (“female brain” or “male brain”). However, such a distinction would be possible only if sex/gender differences in brain features were highly dimorphic (i.e., little overlap between the forms of these features in males and females) and internally consistent (i.e., a brain has only “male” or only “female” features).”

Data from animals showing that the effects of sex can be different and even opposite under different conditions suggest that internal consistency should be poor. As I wrote in

my response to Del Guidice on Sexnet (December 5, 2015), our method of analysis was "specifically designed to test the hypothesis that because the effects of sex can be different and even opposite under different conditions, more brains will have features at the two extremes of the distribution (substantial variability) compared to brains which are always at the same side of the distribution (internally consistent)".

We found that "even when analyses are restricted to a small number of brain regions (or connections) showing the largest sex/gender differences, internal consistency is rare and is much less common than substantial variability (i.e., being at the one end of the "maleness-femaleness" continuum on some elements and at the other end on other elements). This finding was independent of sample, age, type of imaging, method of analysis of the imaging data, and the specific definition of the end of the continuum" (Joel et al., 2015, p. 15472; see also Table S2).

So THE question using our method is: which is more prevalent, substantial variability or internal consistency? Indeed, following my response to Del Guidice on Sexnet, Del Guidice and colleagues added the percent of profiles with substantial variability to all of their analyses. Unfortunately, at some places in their online publication, Del Guidice et al reported only the percent of profiles with internal consistency.

**Del Guidice and colleagues' validation of our methodological approach**

Considering internal consistency and substantial variability, Del Guidice and colleagues provide a very elegant validation of our method, by demonstrating that it can detect a situation in which there are indeed two distinct populations, in this case, different primate species. Thus, with a cutoff of 33%, they found internal consistency in 1.1%-5.1% of profiles and substantial variability in 0% of profiles. So according to our criterion, this should be considered a situation of two distinct populations.

(Obviously with an overlap between species in single facial characteristics of less than 10%, I would have recommended using a higher cutoff, say 90%, which would have yielded a higher percent of internally consistent profiles, but as I stressed above and in

the PNAS paper, what is important is not the absolute proportion of internally consistent profiles but the relations between internal consistency and substantial variability).

So Del Guidice and colleagues reinforce our claim that human brains, in which substantial variability is much more common than internal consistency (regardless of the specific cutoff, Table S2), do not come in two distinct types, as human genitalia (and faces of different primate species) do.

Now that we know that indeed by comparing the occurrence of internal consistency and substantial variability one can detect a situation of two distinct populations, we can look at the results of the simulations. Del Guidice and colleagues demonstrate that our method returns more substantially variable profiles than internally consistent profiles, unless correlations and/or sex/gender differences become extremely large. These simulations thus suggest that it is very unlikely that the categories "male" and "female" extend beyond the genitalia, as it is only under very high correlations or very large sex/gender differences that distinct "male" and "female" types would be found. We hope future studies of additional systems in which sex/gender differences were found (e.g., the immune system) would use our method to determine whether the relations between sex and these systems is better characterized as two distinct populations or as mosaic.

**The question of prediction**

Regarding the ability to predict one's sex category on the basis of the form of one's brain, as I have previously written (starting with Joel, 2011), this can clearly be done, and I am sure with much better accuracy than Del Guidice and colleagues achieved. However, we are interested in the reverse problem – whether one can predict the form of one's brain (or gender) mosaic on the basis of one's sex category. Our analysis of the data suggests that this is not possible.

## On difference and dimorphism

For a discussion of the distinction between sex dimorphism and sex difference see McCarthy and Konkle (2005). In our data there was no measure showing dimorphism, although there were many showing sex/gender differences. In fact, our whole analysis is built on the existence of such differences. So we do not "call into question the very idea of gender differences in brain structure", we only point to the fact that in our data there was no characteristic which was dimorphic.

## An open call to Richard Lippa and the other "owners" of the data from the BBC sex ID study to make their data available to researchers

Although it would have been nice if our new approach to the study of sex had been embraced by everyone, we (the authors of the PNAS paper) believe we should do as much as possible to enable critical discussions around it. Therefore, we have decided to make our processed data available to all, in addition to the raw data, which have been made available according to PNAS guidelines. I hereby call on Richard Lippa, who is one of the authors of Del Guidice et al online publication, and the other "owners" of the BBC sex ID data to make their data available to all researchers, with no a priori conditions. Currently the agreement between the "owners" is that they "would not release the data to outside researchers unless one of us was an active collaborator with that researcher, and we could (and have, in fact, over the years) evaluate requests to analyze the data, or portions of the data. Then, we could accept or not accept such requests, based on our evaluations of the merits of the hypotheses, proposed analyses, qualifications of the researchers" (cited from an email sent to me on December 10, 2015, by Lippa, in response to my request for his permission to use the data).

**References:**

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