Author’s response to reviews

Title: Neurocognitive impact of metal exposure and social stressors among schoolchildren in Taranto, Italy.

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Author’s response to reviews:

Dear Reviewers,
Thank you for your valuable feedback on our manuscript. We sincerely appreciate your contributions towards the improvement of our article. In this letter, we respond to your suggestions and comments with the goal of fully addressing each of them.

Reviewer #2:

Comment 12:
I think this paragraph should be included after SES and before home environment measures.
Done.

Comment 16:
SES: spell out in abstract too.
Page 6, line 44: use "SES" instead of "socio-economic status".
Amended.

Comment 19:
Specify the executive functions measured by these instruments.
Added information about executive functions.

Comment 32:
Why these variables and not others? How were they chosen?
Clarified: “In addition to the effect of the exposure biomarkers and SES all regression models were adjusted for the covariates that we hypothesize to influence cognitive functions like sex, age, maternal non-verbal intelligence and cognitive stimulation besides the confounder distance from the point source.”
Comment 33:

Please, provide the score ranges, we don’t know if 5 points is little or big change.

Amended: “The SES resulted associated with the IQ score, with lowest levels showing IQ, GAI and WMI of about 5 points lower than the highest SES level, and VCI around 7 points lower than the highest SES level (IQ: βhigh SES 4.8; GAI: βhigh SES 5.6; WMI: βhigh SES 5.3; VCI: βhigh SES 7.1) which means a relative percentage change of about 6%, 7% and 9% respectively, considering the ranges of the three cognitive outcomes ((64, 143), (61, 139), (64, 144) respectively).”

Comment 38:

"A significant difference among the SES levels resulted for WMI, for which we found a null effect of BPb at the medium (β 0.6; 95% CI -1.9, 3.1) and high SES levels (β 1.0; 95% CI -2.6, 4.6) when modifying the contrast matrix".

Different values in table.

Clarify the meaning of "when modifying the contrast matrix".

Amended: We decided to remove this part to avoid any confusion since these were not main results and they were not significant.

Comment 39:

"This study revealed a marked reduction of about 15 IQ points…"

"The IQ total score and all sub-scores, except PSI, were inversely related to the distance from the point source which may indicate a potential role of the exposure to industrial emissions."

Is this based on descriptive analyses? Not main result, I think this should be removed.

Done.

"When considering metal exposure and subjects SES we found that subjects with higher SES showed to have better neurocognitive scores and the effect of metal exposure was enhanced when subjects had a lower SES, in particular a higher BPb exposure for subjects in the lower SES was associated with a statistically significant lower WMI".

This part should be rewritten, from my point of view, it’s not clear.
Amended: “This study revealed that subjects with higher SES showed better neurocognitive scores compared to those with lower SES. A significant interaction of metal exposure with SES was also observed: a higher BPb level for subjects in the lower SES was associated with a statistically significant lower WMI”.

Comment 41:

"Significant associations resulted instead between some of the CANTAB scores and BPb and HMn, with BPb lower the proportion of successful stops and higher the stop signal reaction time in the SST tests, and HMn higher the between errors in the SWM tests”.

This sentence is not correct, use lower and higher properly.

Amended: “Significant associations resulted between some of the CANTAB scores and BPb and HMn, with a lower proportion of successful stops and higher stop signal reaction time in the SST tests at increasing BPb, and higher between errors in the SWM tests at increasing HMn.”

Comment 42:

"The CANTAB tests are designed to target more specific executive functions, whereas the WISC-IV examines more general composite scores of neuro-cognitive abilities.

This may explain why associations with the exposure biomarkers were more evident for the CANTAB tests than for the IQ total and sub-scores, for which the effect of metal exposure may be mitigated by other factors."

Specify other factors.

Specified: “The CANTAB tests are designed to target more specific executive functions, whereas the WISC-IV examines more general composite scores of neuro-cognitive abilities. This may explain why associations with the exposure biomarkers were more evident for the CANTAB tests than for the IQ total and sub-scores, for which the effect of metal exposure may be mitigated by other factors like verbal intelligence or perceptual reasoning.”

Best regards,

Stefano Renzetti and co-authors