ADNI Alzheimer's Disease Neuroimaging Initiative

ADNI DOD1: first batch analysis of CSF biomarkers

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Summary

A total of 69 BASELINE CSF aliquot samples, never before thawed aliquots of ADNI DOD1 study subjects were tested in a total of 5 analytical runs. . Each calibration standard sample, quality control sample and ADNI DOD1 study subject sample were run in duplicate according to the manufacturer's instructions. Each test result is the mean value of the duplicates. The attached "ADNI DOD report" provides details for the analyses including calibrator and quality control samples performance, and the raw data for these analyses. The accompanying DOD1 ADNI 2 2014 CSF $A\beta_{1\text{-}42}$, t-tau and p-tau_{181} dataset in .csv file format (DOD1 UPENNBIOMK1) provides the final set of results following rescaling (Transformation) based on 2012/13 BASELINE ADNI results, according to the procedure described below, for the 2014 DOD1 ADNI II CSF sample analyses. In addition, the DOD1 UPENNBIOMK1 data file includes the RAW untransformed data.

Method

The xMAP Luminex platform and Innogenetics/Fujirebio AlzBio3 immunoassay kits were used following the SOP in place at the UPenn/ADNI Biomarker Laboratory, according to the kit manufacturer's instructions and as described in previous publications (1-4). Analyses were performed in a series of 5 runs using a 96 well plate format, over the time period of October 23 through November 7, 2014 using standards and kit lot#s: S236947-K242298. Acceptance criteria as documented in the UPenn/ADNI Biomarker Laboratory SOP were followed for these analyses.

Each of the 5 analytical runs met acceptance criteria for calibrator precision and accuracy (back calculated concentration result vs nominal concentration result) and quality control results were within stated limits (detailed data in "ADNI DOD report"). Individual sample results were acceptable in all cases except for a single tau and a single p-tau_{181} result, where noted, and that was reported as "NA" in the .CSV file "DOD1 UPENNBIOMK1".

In order to assure cross-sectional comparability of results between these DOD1 subject CSF samples and the earlier 2012/13 BASELINE CSF biomarker results, assessment of the concentrations of $A\beta_{1\text{-}42}$, t-tau and p-tau_{181} were performed in a set of 31 never before thawed ADNI GO and II patient BASELINE CSF aliquots ("sister" pristine aliquots had previously been run in the 2012 or the 2013 batch runs and new pristine aliquots were included in the first 31 series of ongoing longitudinal sample sets from ADNI GO and II subjects run in the December-January 2014-2015 batch run using the same batch of standards and kit reagent lot numbers: S236947-K242298 as used for the DOD1 batch). Linear regression analyses (Passing-Bablok) were performed for $A\beta_{1\text{-}42}$, t-tau and p-tau_{181} comparing RAW CSF concentration results obtained

in ADNI GO and II, Dec 2014 with those obtained in the analyses performed in 2012/13(referred in Figure 2 of the ADNI 2: third batch analyses of CSF biomarkers Methods report as "2013T") transformed to 2007 BASELINE as described in UPENNBIOMK5) (see Figure 2 in the Methods report "ADNI 2 third batch analyses" for UPENNBIOMK7). For $A\beta_{1-42}$ the slope value is 1.474 and y-intercept value is -41.9 pg/mL, for t-tau the slope value is 0.86 and y-intercept is 1.96 pg/mL and for p-tau_{181} the slope is 0.44 and y-intercept is 7.6. The slope and intercept values were then used to bridge between the 2012/13 data and the current DOD1 2014 CSF concentrations. This was accomplished by solving the equation, X = (Y-b)/m (X is the rescaled (Transformed) 2012 or 2013 result; Y is the raw DOD1 2014 result; m is the slope of the regression analysis and b is the Y intercept value of the regression analysis summarized in Figure 2). For studies that use 2014 DOD1 CSF biomarker concentration results, we recommend the use of the transformed results. As noted in the Summary the raw data can be found in the DOD1 UPENNBIOMK1 dataset csv file and is also presented in the analytical report entitled "ADNI DOD report ".

References

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