Poster WePe12.6C05
3rd IAS Conference on HIV Pathogenesis and Treatment
24-27 July 2005, Rio de Janeiro, Brazil

Treatment history data significantly increase the accuracy of neural networks in predicting virological response to combination therapy

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Introduction

- Standard genotyping tests have limited sensitivity (≥20%) for detecting minority resistant virus
- Artificial Neural Networks (ANN) can successfully predict virological response to combination antiretroviral therapy from genotype but undetected minority resistant species might limit their accuracy
- This study addresses whether inclusion of treatment history data improves the accuracy of ANN.

Methods

- Two committees of 10 ANN models were trained to predict virological response (ΔVL) to combination antiretroviral therapy from genotype and other input variables using 2,559 treatment change episodes (TCEs)
- The 'basic' committee models were trained using the following input variables: baseline viral load, drugs in new regimen, mutations (55 resistance mutations) and time to follow-up
- The 'treatment history models' were trained with the above input variables plus four additional treatment history variables, coded as '0' or '1' for any previous:
  1. AZT (as a surrogate for possible thymidine analogue-associated mutations)
  2. 3TC (because of the well-documented effects of the signature M184V mutation)
  3. NNRTIs (because of the substantial cross resistance between these inhibitors)
  4. PIs (because of the moderate cross resistance between these inhibitors)

  These variables were used in order to limit the number of additional variables while testing the hypothesis across all three major classes of current drugs.
- The ANN committees were tested by being given the input variables from 51 independent TCEs, selected at random from different patients within the RDI database, and predicting ΔVL
- The 'committee average prediction' was used (the average prediction of all 10 models in the committee for each test TCE)
- The models' performance was assessed by comparing these predictions to the actual ΔVL from the test TCEs in terms of:
  1. Correlations (Pearson's Product-Moment) between the ANN models' predictions and the actual ΔVL values
  2. The mean absolute difference between the models' predictions and the ΔVL
  3. The percentage of the models' predictions that had the correct trajectory, positive or negative.

NB a detailed description of the methodology by which ANN committees are developed is presented in Poster WePe12.6CO4.

Results

- Correlations between predicted and actual ΔVL produced r^2 values of 0.30 ($p<0.0001$) for the basic models and 0.45 ($p<0.00001$) for the treatment history models. The difference in performance was statistically significant ($p<0.05$)
- The mean absolute difference between predicted and actual ΔVL was 0.88 for the basic models and 0.78 for the treatment history models ($p=0.05$)
- The mean percentage of correct trajectory predictions was 76% for the basic models and 78% for the treatment history models ($p<0.05$).

These results are summarised in Table 1 and the scatterplots of the correlations between the predicted and actual ΔVL values are presented in Figures 1 and 2.

Table 1: Summary of results

	Correlation (r^2)	Mean absolute difference score	Percentage correct trajectory predictions
Basic models	0.30	0.88	76%
Treatment history models	0.45	0.78	78%
Statistical significance*	$p<0.01$	$p=0.05$	$p<0.05$

* For correlations and mean percentage correct trajectory predictions, the scores for the ten individual ANN models within each committee were compared using a two-tailed t-test for unrelated samples. For the absolute difference scores the committee average predictions for each TCE were compared using a two-tailed t-test for paired samples.

Figure 1: Scatterplot of predicted vs actual ΔVL for basic ANN models

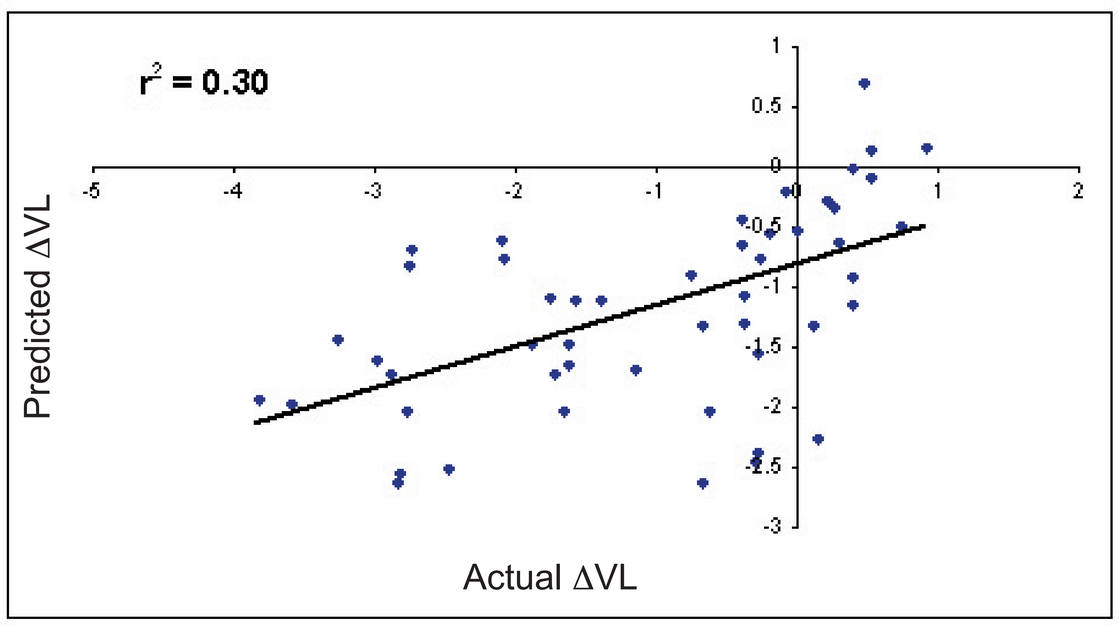
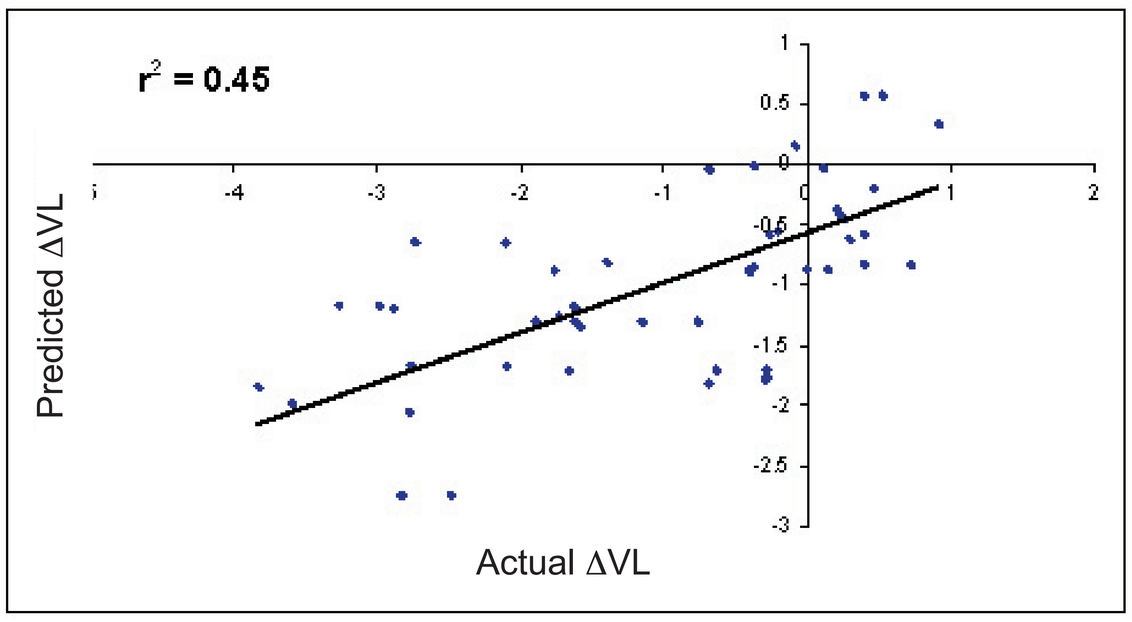


Figure 2: Scatterplot of predicted vs actual ΔVL for treatment history ANN models



Conclusions

- **Treatment history data significantly improved the accuracy of ANN in predicting virological response to combination antiretroviral therapy**
- **Visual inspection of the scatterplots indicates this was largely due to a reduction in the number of cases where the models predicted a greater virological reponse than actually achieved**
- **The treatment history data may have acted as a surrogate for minority populations of resistant virus that undermined subsequent therapy**

Acknowledgments

The RDI thanks:
- NIAID and the US Military HIV Research Program and the BC Centre for Excellence in HIV/AIDS for their support and collaboration with this research
- All the centres around the world that have contributed data
- The patients

This project has been funded with Federal Funds from the National Cancer Institute, National Institutes of Health, under contract No. NO1-CO-12400 and from the US Military HIV Research Program (under the Army Cooperative Agreement No. W81XWH-014-2-0005).