Treatment History and Adherence Information Significantly Improves Prediction of Virological Response by Neural Networks

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hiv resistance response database initiative

Poster 52

14th International Drug Resistance Workshop
Quebec, Canada; June 7-11, 2005

Introduction

- Standard genotyping tests have limited sensitivity for detecting minority resistant virus
- Artificial Neural Networks (ANN) can successfully predict virologic response to HAART from genotype but minority species might limit their accuracy
- Non-adherent patient training data could also reduce ANN accuracy (e.g., causing incorrect predictions of virologic failure despite a 'benign' genotype)
- Current studies addressed whether inclusion of treatment history data & censoring training data for adherence improve the accuracy of ANN.

Methods

Four studies were conducted - in each, 'committees' of 10 ANN models were trained to predict virologic response (ΔVL) to treatment, as detailed on Poster 53 (Wegner, S *et al*):

1. Two committees trained using 2,559 treatment change episodes (TCEs)
   - 'Basic' committee training variables: baseline viral load, drugs, mutations (55) & time to follow-up
   - 'Treatment history' committee also trained with treatment history variables (AZT, 3TC, any NNRTI & any PI)
2. Two committees were trained using the basic input variables with data from patients (n=623 TCEs) with low & high (< or ≥90%) adherence (estimated by prescription re-fills)
3. A committee was trained using data from adherent patients (n=495 TCEs), plus the additional treatment history variables
4. A committee was trained using data from adherent patients (n=495 TCEs) & a reduced set of 36 mutation input variables (those with greatest impact on virological response), plus the additional treatment history variables

ANN models were tested by being given the input variables from independent data (n=51 for study 1, n=50 for study 2 and n=47 for studies 3 & 4) & predicting ΔVL. The models' performance was assessed using the 'committee average prediction' (the average prediction of all 10 models for each test TCE).

Results

The results from all four studies are summarised in Table 1.

Study 1: Treatment history

Treatment history models were more accurate than the basic models:

- Correlations between predicted & actual ΔVL: r^2=0.45 *vs* 0.30 (p<0.01) (Figure 1)
- Mean absolute difference (predicted *vs* actual ΔVL): 0.78 *vs* 0.88 (p=0.05)
- VL trajectory predictions: 78% correct *vs* 76% (p<0.05).

Table 1: Summary of results

		Correlation (r^2)	Mean absolute difference	Mean trajectory score
Study 1: Treatment history	Basic models	0.30	0.88	76%
	Treatment history	0.45	0.78	78%
	Stat. significance*	p<0.01	p=0.05	p<0.05
Study 2: Adherence	Basic models	0.11	1.16	78%
	Low adherence	0.29	0.94	84%
	Stat. significance	p<0.01	p<0.01	ns
Study 3: Treatment history + high adherence		0.24	0.95	79%
Study 4: As per Study 3 + reduced mutations		0.46	0.76	87%
Statistical significance (Study 3 *vs* 4)		p<0.001	p<0.01	ns

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

Study 2: Adherence

The 'high-adherence' models performed more accurately than the 'low-adherence' models:

- r^2: 0.29 vs 0.11 (p<0.01) (Figure 2)
- Mean absolute difference scores: 0.94 vs 1.16; p<0.01
- VL trajectory predictions: 84% correct vs 78% (ns).

Figure 1: Correlations between predicted and actual ΔVL for basic and treatment history ANN models

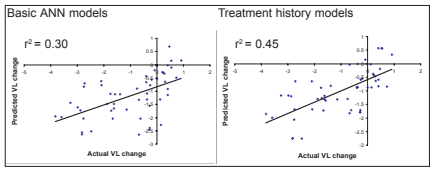
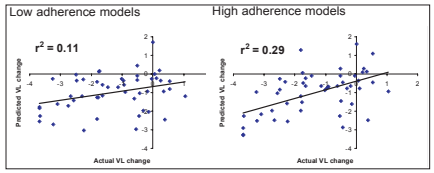


Figure 2: Correlations between predicted and actual ΔVL for low and high adherence ANN models



Study 3: Treatment history + high adherence

These ANN models performed at an intermediate level:

- r^2: 0.24
- Mean absolute difference score: 0.95
- Trajectory: 79%.

Study 4: Treatment history + high adherence + reduced mutation set

These ANN models with a reduced mutation set showed improved performance:

- r^2: 0.46
- Mean absolute difference score: 0.76
- Correct trajectory: 87%.

Conclusions

- **Treatment history data significantly improved the accuracy of ANN in predicting virological response - possibly acting as a 'surrogate' for minority mutant populations**
- **ANN models trained using data from highly adherent patients were significantly more accurate than those trained with data from less adherent patients**
- **Initial combined 'treatment history/adherent' models achieved an intermediate level of performance - possibly due to the relatively small training set (n=495) & large number of input variables (75)**
- **Combined models trained using a reduced mutation set had improved performance**
- **These data indicate that the RDI programme of ANN model refinement is leading to improvements in predictive accuracy but that increases in the number of input variables may require larger datasets from adherent patients to achieve more optimum performance.**

Acknowledgments

The RDI thanks NIAID, the US Military HIV Research Program and the BC Centre for Excellence for their support and collaboration with this research and all those centres around the world that have contributed data.

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).