Contents - Chapter 3

Results

RESULTS CHAPTER

3.1 Patient demographics for melatonin data analysis.

Age	49 +/- 10.3
BMI	29 +/- 5.2
Total RDI	14 +/- 22.4
RDI NREM	15.0 +/- 25.0
RDI REM	19.7 +/- 22.4
Min sat% NREM	86.4 +/- 14.9
Min sat% REM	86. +/- 8.7
Total arousal index/hr	29.3 +/- 22.7

All data is expressed as mean +/- standard deviation.

The demographic data demonstrates a satisfactory spread of ages. The spread of values for the parameters of sleep disordered breathing suggest that an adequate patient sample was obtained for data analysis.

3.2 Melatonin Data Analysis.

3.2.1 Simple linear regression of urinary production of 6-sulphatoxymelatonin versus variables of sleep disordered breathing.

Both diurnal and nocturnal urinary metabolite levels were analysed by simple linear regression against NREM and REM RDI as well as total RDI and the arousal index. Analysis was also performed in the same fashion against parameters of hypoxia including the lowest saturation in REM and NREM sleep. The data for all variables is presented in table form below.

Regression Summary
Total Urine 6-sulphatoxymelatonin (nmol) Nocturnal vs. RDI REM

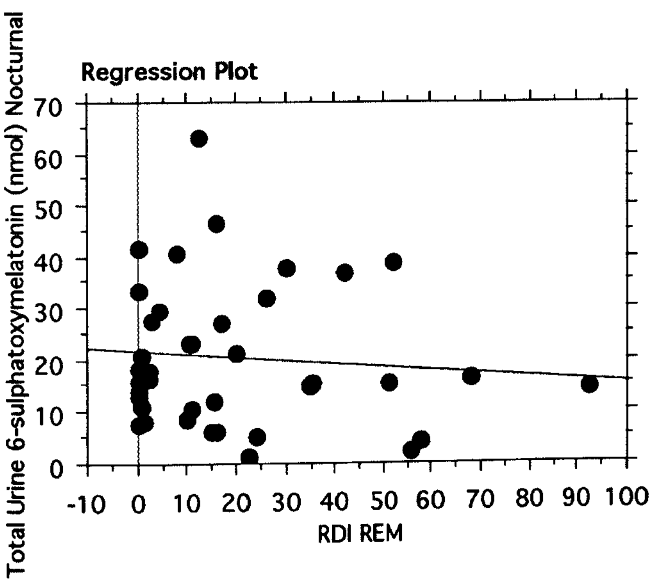
Count	39
Num. Missing	1
R	.102
R Squared	.010
Adjusted R Squared	•
RMS Residual	14.010

ANOVA Table
Total Urine 6-sulphatoxymelatonin (nmol) Nocturnal vs. RDI REM

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Regression	1	76.487	76.487	.390	.5363
Residual	37	7262.516	196.284		
Total	38	7339.003			

Regression Coefficients
Total Urine 6-sulphatoxymelatonin (nmol) Nocturnal vs. RDI REM

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	21.845	3.006	21.845	7.266	<.0001
RDI REM	-.063	.102	-.102	-.624	.5363



Y = 21.845 - .063 * X; R^2 = .01

Regression Summary
Total Urine 6-sulphatoxymelatonin (nmol) Nocturnal vs. RDI NREM

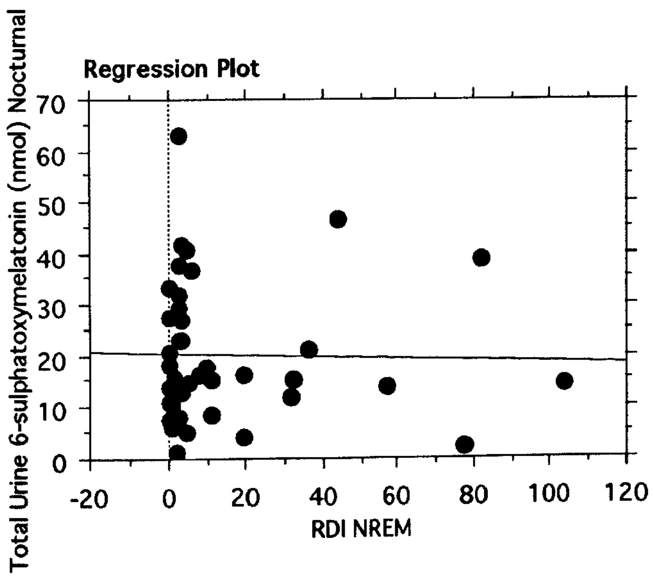
Count	40
Num. Missing	0
R	.030
R Squared	.001
Adjusted R Squared	•
RMS Residual	13.928

ANOVA Table
Total Urine 6-sulphatoxymelatonin (nmol) Nocturnal vs. RDI NREM

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Regression	1	6.835	6.835	.035	.8521
Residual	38	7371.293	193.981		
Total	39	7378.129			

Regression Coefficients
Total Urine 6-sulphatoxymelatonin (nmol) Nocturnal vs. RDI NREM

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	20.689	2.577	20.689	8.027	<.0001
RDI NREM	-.017	.089	-.030	-.188	.8521



Y = 20.689 - .017 * X; R^2 = .001

Regression Summary
Total Urine 6-sulphatoxymelatonin (nmol) Nocturnal vs. Min Sat%(REM)

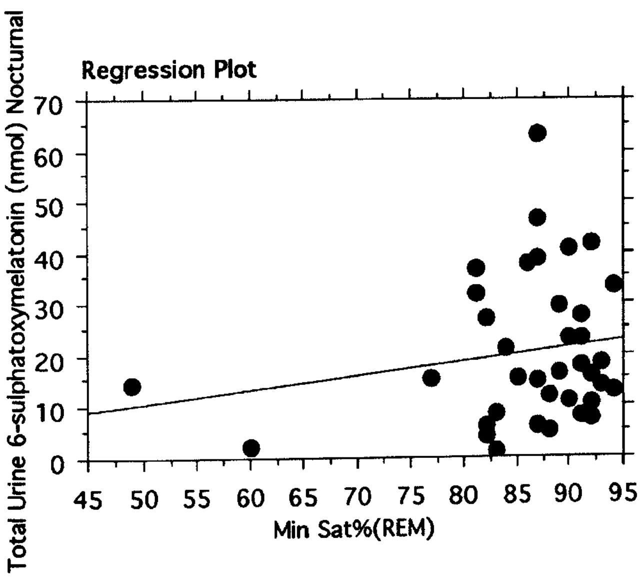
Count	38
Num. Missing	2
R	.172
R Squared	.030
Adjusted R Squared	.003
RMS Residual	14.065

ANOVA Table
Total Urine 6-sulphatoxymelatonin (nmol) Nocturnal vs. Min Sat%(REM)

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Regression	1	217.346	217.346	1.099	.3015
Residual	36	7121.577	197.822		
Total	37	7338.923			

Regression Coefficients
Total Urine 6-sulphatoxymelatonin (nmol) Nocturnal vs. Min Sat%(REM)

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	-3.358	22.959	-3.358	-.146	.8845
Min Sat%(REM)	.278	.266	.172	1.048	.3015



Y = -3.358 + .278 * X; R^2 = .03

Regression Summary
Total Urine 6-sulphatoxymelatonin (nmol) Nocturnal vs. Min Sat%(NREM)

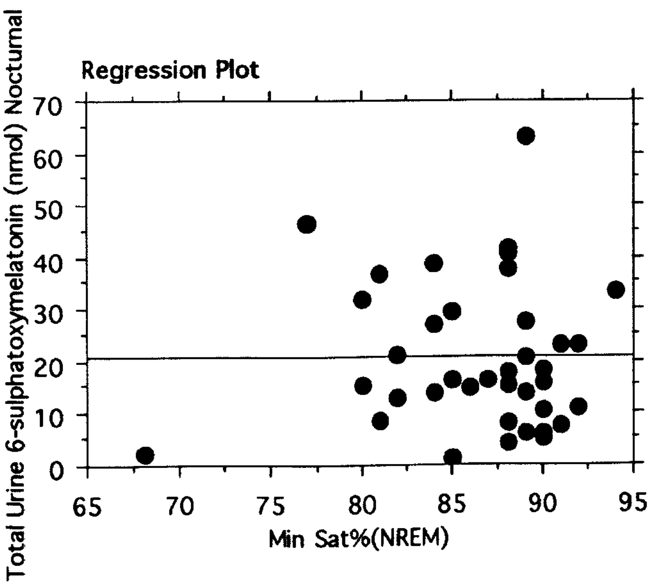
Count	38
Num. Missing	2
R	.002
R Squared	2.741E-6
Adjusted R Squared	•
RMS Residual	14.210

ANOVA Table
Total Urine 6-sulphatoxymelatonin (nmol) Nocturnal vs. Min Sat%(NREM)

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Regression	1	.020	.020	9.867E-5	.9921
Residual	36	7268.968	201.916		
Total	37	7268.988			

Regression Coefficients
Total Urine 6-sulphatoxymelatonin (nmol) Nocturnal vs. Min Sat%(NREM)

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	21.214	40.775	21.214	.520	.6061
Min Sat%(NREM)	-.005	.471	-.002	-.010	.9921



Y = 21.214 - .005 * X; R^2 = 2.741E-6

Regression Summary
Total Urine 6-sulphatoxymelatonin (nmol) Nocturnal vs. RDI

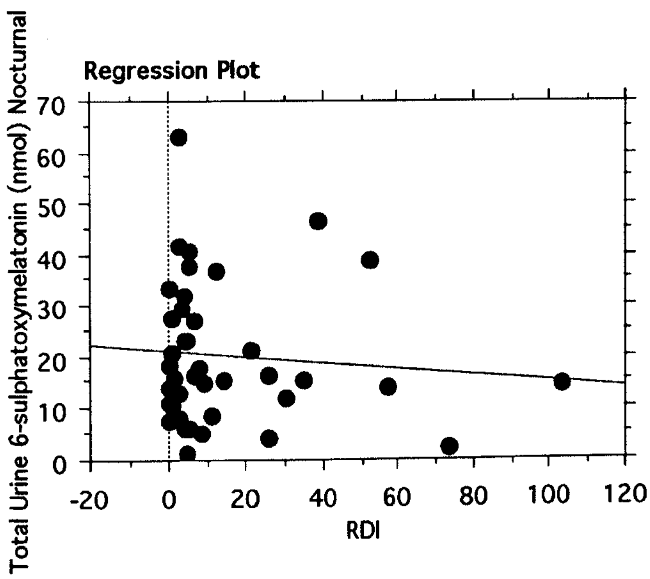
Count	40
Num. Missing	0
R	.098
R Squared	.010
Adjusted R Squared	•
RMS Residual	13.867

ANOVA Table
Total Urine 6-sulphatoxymelatonin (nmol) Nocturnal vs. RDI

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Regression	1	70.810	70.810	.368	.5476
Residual	38	7307.319	192.298		
Total	39	7378.129			

Regression Coefficients
Total Urine 6-sulphatoxymelatonin (nmol) Nocturnal vs. RDI

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	21.331	2.641	21.331	8.076	<.0001
RDI	-.060	.099	-.098	-.607	.5476



Y = 21.331 - .06 * X; R^2 = .01

Regression Summary
Total Urine 6-sulphatoxymelatonin (nmol) Nocturnal vs. AI

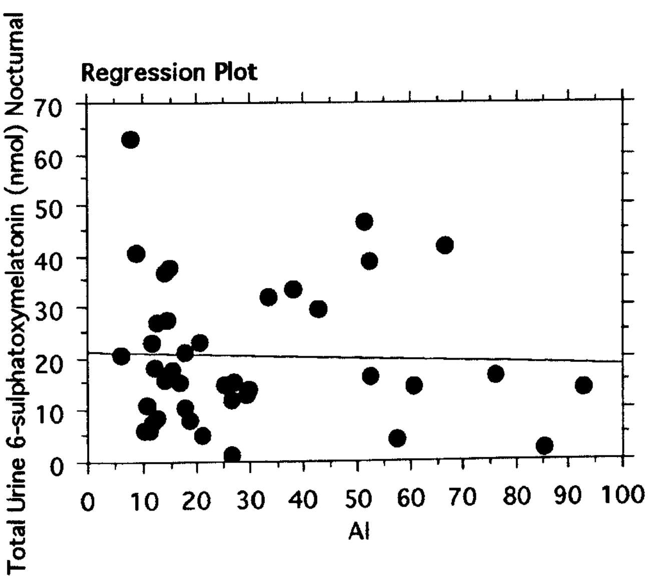
Count	40
Num. Missing	0
R	.046
R Squared	.002
Adjusted R Squared	•
RMS Residual	13.920

ANOVA Table
Total Urine 6-sulphatoxymelatonin (nmol) Nocturnal vs. AI

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Regression	1	15.525	15.525	.080	.7787
Residual	38	7362.604	193.753		
Total	39	7378.129			

Regression Coefficients
Total Urine 6-sulphatoxymelatonin (nmol) Nocturnal vs. AI

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	21.250	3.617	21.250	5.876	<.0001
AI	-.028	.098	-.046	-.283	.7787



Y = 21.25 - .028 * X; R^2 = .002

Regression Summary
Total Urine 6-sulphatoxymelatonin (nmol) Diurnal vs. RDI REM

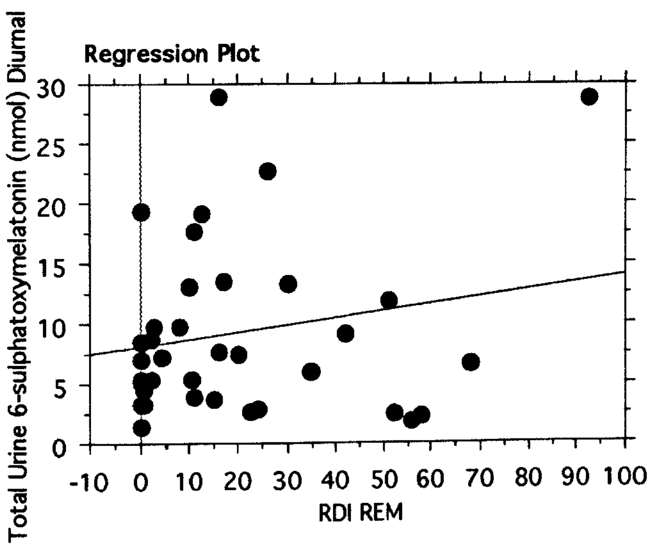
Count	36
Num. Missing	4
R	.186
R Squared	.035
Adjusted R Squared	.006
RMS Residual	7.173

ANOVA Table
Total Urine 6-sulphatoxymelatonin (nmol) Diurnal vs. RDI REM

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Regression	1	62.809	62.809	1.221	.2769
Residual	34	1749.177	51.446		
Total	35	1811.987			

Regression Coefficients
Total Urine 6-sulphatoxymelatonin (nmol) Diurnal vs. RDI REM

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	8.032	1.592	8.032	5.044	<.0001
RDI REM	.058	.053	.186	1.105	.2769



Y = 8.032 + .058 * X; R^2 = .035

Regression Summary
Total Urine 6-sulphatoxymelatonin (nmol) Diurnal vs. RDI NREM

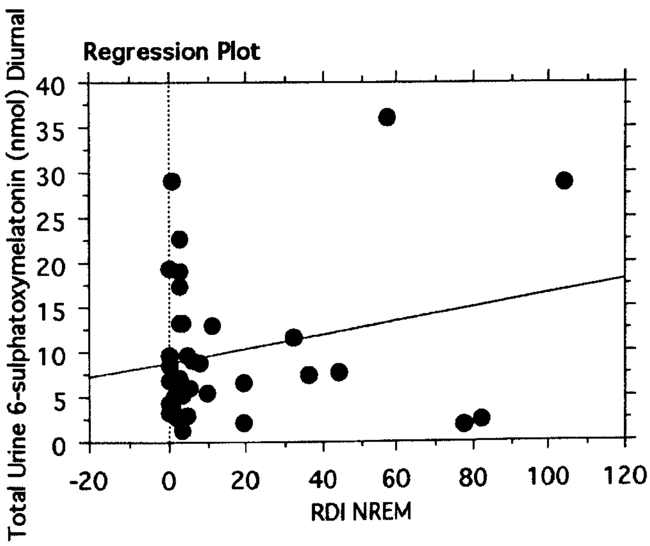
Count	37
Num. Missing	3
R	.237
R Squared	.056
Adjusted R Squared	.029
RMS Residual	8.230

ANOVA Table
Total Urine 6-sulphatoxymelatonin (nmol) Diurnal vs. RDI NREM

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Regression	1	141.448	141.448	2.088	.1573
Residual	35	2370.546	67.730		
Total	36	2511.994			

Regression Coefficients
Total Urine 6-sulphatoxymelatonin (nmol) Diurnal vs. RDI NREM

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	8.767	1.570	8.767	5.583	<.0001
RDI NREM	.077	.053	.237	1.445	.1573



Y = 8.767 + .077 * X; R^2 = .056

Regression Summary
Total Urine 6-sulphatoxymelatonin (nmol) Diurnal vs. Min Sat%(REM)

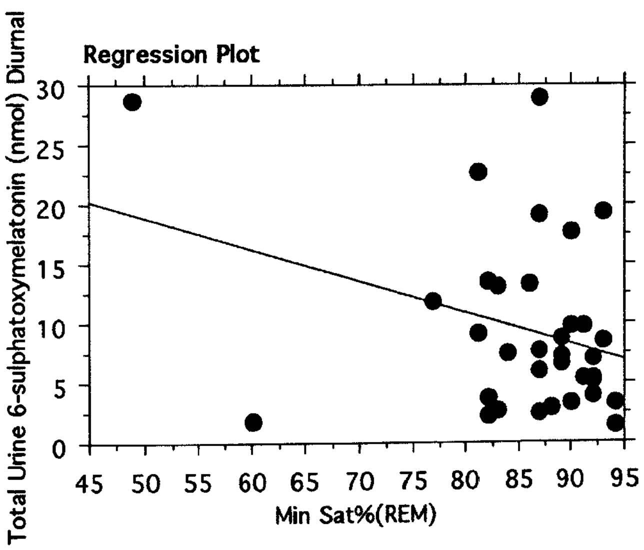
Count	35
Num. Missing	5
R	.334
R Squared	.111
Adjusted R Squared	.085
RMS Residual	6.941

ANOVA Table
Total Urine 6-sulphatoxymelatonin (nmol) Diurnal vs. Min Sat%(REM)

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Regression	1	199.461	199.461	4.140	.0500
Residual	33	1589.964	48.181		
Total	34	1789.425			

Regression Coefficients
Total Urine 6-sulphatoxymelatonin (nmol) Diurnal vs. Min Sat%(REM)

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	32.350	11.375	32.350	2.844	.0076
Min Sat%(REM)	-.268	.132	-.334	-2.035	.0500



Y = 32.35 - .268 * X; R^2 = .111

Regression Summary
Total Urine 6-sulphatoxymelatonin (nmol) Diurnal vs. Min Sat%(NREM)

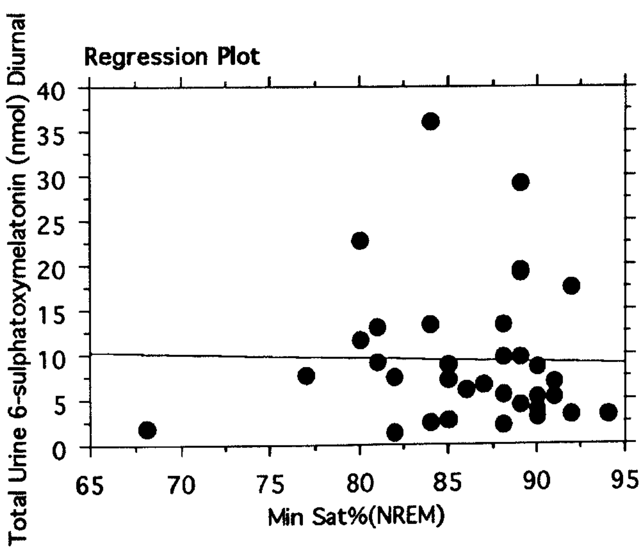
Count	36
Num. Missing	4
R	.028
R Squared	.001
Adjusted R Squared	•
RMS Residual	7.943

ANOVA Table
Total Urine 6-sulphatoxymelatonin (nmol) Diurnal vs. Min Sat%(NREM)

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Regression	1	1.637	1.637	.026	.8730
Residual	34	2145.223	63.095		
Total	35	2146.859			

Regression Coefficients
Total Urine 6-sulphatoxymelatonin (nmol) Diurnal vs. Min Sat%(NREM)

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	13.069	22.842	13.069	.572	.5710
Min Sat%(NREM)	-.043	.264	-.028	-.161	.8730



Y = 13.069 - .043 * X; R^2 = .001

Regression Summary
Total Urine 6-sulphatoxymelatonin (nmol) Diurnal vs. RDI

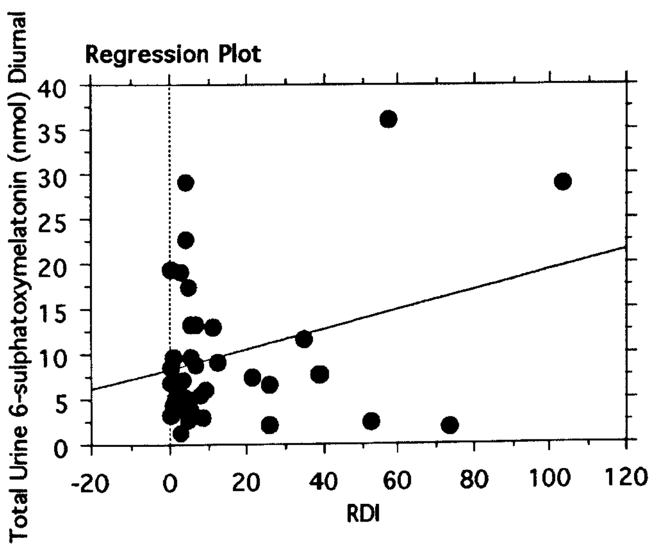
Count	37
Num. Missing	3
R	.299
R Squared	.089
Adjusted R Squared	.063
RMS Residual	8.085

ANOVA Table
Total Urine 6-sulphatoxymelatonin (nmol) Diurnal vs. RDI

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Regression	1	224.335	224.335	3.432	.0724
Residual	35	2287.659	65.362		
Total	36	2511.994			

Regression Coefficients
Total Urine 6-sulphatoxymelatonin (nmol) Diurnal vs. RDI

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	8.322	1.584	8.322	5.252	<.0001
RDI	.108	.058	.299	1.853	.0724



Y = 8.322 + .108 * X; R^2 = .089

Regression Summary
Total Urine 6-sulphatoxymelatonin (nmol) Diurnal vs. AI

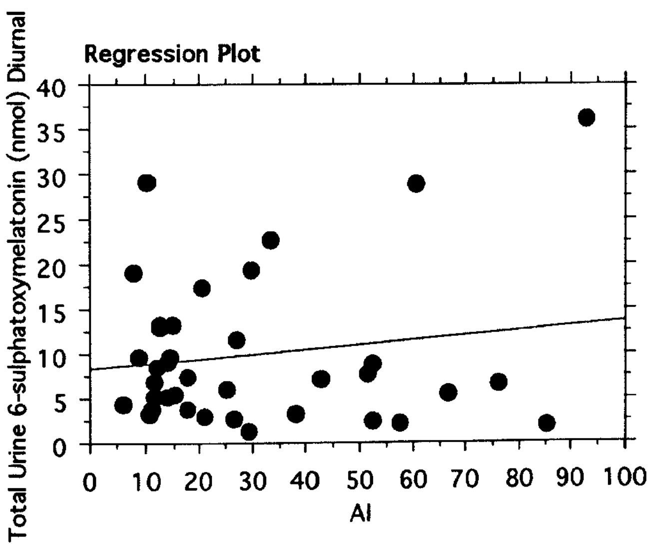
Count	37
Num. Missing	3
R	.147
R Squared	.022
Adjusted R Squared	•
RMS Residual	8.380

ANOVA Table
Total Urine 6-sulphatoxymelatonin (nmol) Diurnal vs. AI

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Regression	1	54.241	54.241	.772	.3855
Residual	35	2457.753	70.222		
Total	36	2511.994			

Regression Coefficients
Total Urine 6-sulphatoxymelatonin (nmol) Diurnal vs. AI

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	8.353	2.252	8.353	3.708	.0007
AI	.052	.060	.147	.879	.3855

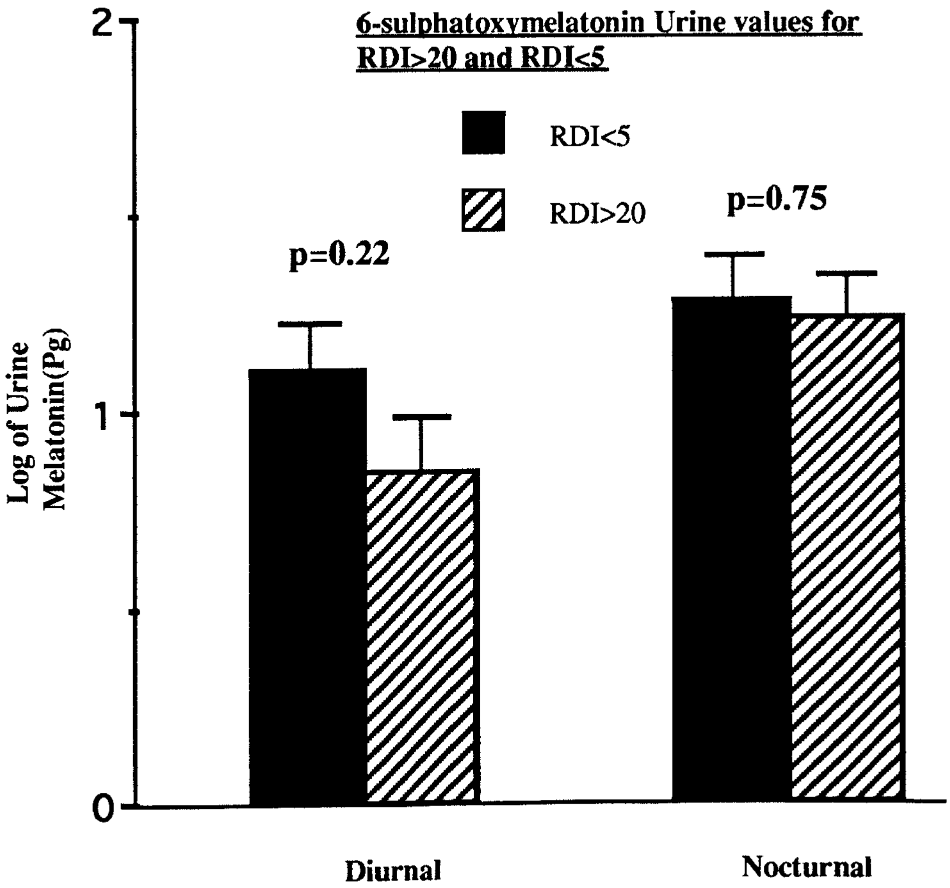


Y = 8.353 + .052 * X; R^2 = .022

The results demonstrate that no relationship exists between the diurnal or nocturnal production of melatonin, as measured by urinary metabolite and the magnitude of sleep disordered breathing as defined by standard criteria.

3.2.2 Unpaired t-testing of apnoeic (RDI>20) versus non-apnoeic (RDI<5) patient groups.

Despite the lack of a direct correlation between the magnitude of SDB, a subsequent analysis between subjects with moderate to severe OSA (RDI>20) and those within the clinical normal range (RDI<5) was performed to explore the possibility of a relationship existing between the severity of OSA and melatonin production which was not evident from the linear regression data. The graph below demonstrates there is no difference between nocturnal or diurnal melatonin production between these two groups by unpaired t-testing. The urinary values have been logged for presentation purposes to overcome the large differences between daytime and night time production of the hormone.



SUMMARY OF MELATONIN DATA

The findings of this arm of the study do not support the hypothesis that abnormal production of melatonin occurs as a result of sleep disordered breathing, and is thus unlikely to play a key role in the genesis of daytime somnolence in this condition.

3.3 Patient demographics for cognitive data analysis.

Age	51 +/- 12
Level of education (years)	15 +/- 3
BMI	29.1 +/- 4.4
Total RDI	14. +/- 19.1
RDI NREM	12.5 +/- 19.2
RDI REM	22.9 +/- 24
Min sat% NREM	86.2 +/- 5.4
Min sat% REM	84.4 +/- 6.8
Total Sleep time(min)	307.9 +/- 56.4
Total arousal index/hr	29.3 +/- 14.5
Estimated WAIS Full Scale IQ from Shipley	114 +/- 12

All data is expressed as mean +/- standard deviation

The majority of patients had received education up to high school (10 - 12 years) although the mean IQ suggests they were an above average group for intelligence. The data with respect to NREM and REM RDI as well as arousal index demonstrates a spread of values ranging between severe OSA and patients without clinical sleep disordered breathing and suggests that a suitable range of subjects was enrolled for the study.

3.4 Simple regression analysis of cognitive variables versus variables of hypoxia.

For ease of presentation, and in light of the large number of regression analyses only those correlations which reached statistically significant values ($P < 0.05$) are presented in of the following chapters. Remaining correlations are presented in Appendix 1 The major findings are presented in the following table including those for Chapter 3.5.1 (total arousal index versus cognitive outcomes). Correlation matrices for each relationship are discussed in detail in each sub-chapter.

Simple regression correlates

Cognitive test	Variable of sleep disordered breathing	p value	r squared	correl -ation
Logical memory I	Arousal index	0.05	0.13	-
Logical memory II	Arousal index	0.05	0.15	-
Logical memory I	NREM RDI	0.02	0.09	-
Logical memory II	NREM RDI	0.01	0.10	-
Logical memory I	Log desat% <90	0.05	0.09	-
Logical memory II	Log desat% <90	0.01	0.14	-
Logical memory II	Total RDI	0.04	0.08	-
Symbol digit	Total RDI	0.03	0.08	-
Symbol digit	RDI REM	0.05	0.15	-
PASAT	Total RDI	0.02	0.10	-
PASAT	NREM RDI	0.02	0.11	-
PASAT	Min. sat% NREM	0.02	0.11	-
PASAT	Min. sat% REM	0.03	0.10	-
Digitspan reverse	Log desat% <90	0.05	0.09	-
Epworth scale	Arousal index	0.03	0.09	-
Steer Clear	Log desat% <90	0.04	0.10	-
COWA	Arousal Index	0.03	0.08	+

The table demonstrates 17 statistically significant results by simple linear regression out of 147 performed. This is in excess of that which would be likely to occur by chance for the given number of variables suggesting they cannot readily be put down to Type I error. All of the associations in the above table have clinical explanations with the exception of COWA versus AI. This final relationship is counter intuitive and therefore thought to be spurious.

3.4.1 Cognitive outcomes versus NREM RDI.

Regression Summary
RDI NREM vs. Logical MP 1

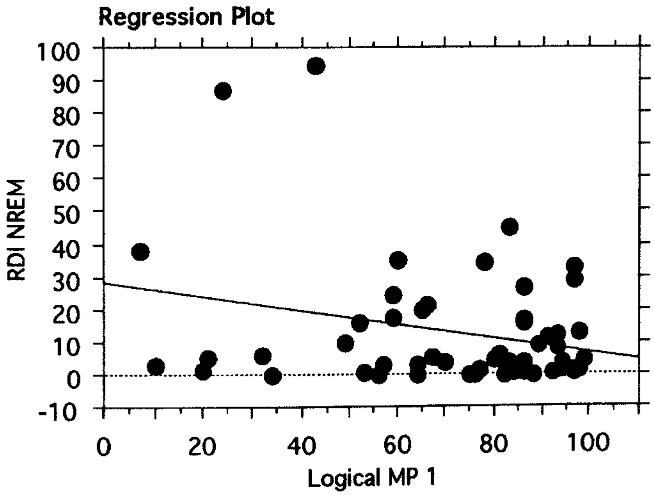
Count	55
Num. Missing	0
R	.282
R Squared	.079
Adjusted R Squared	.062
RMS Residual	18.564

ANOVA Table
RDI NREM vs. Logical MP 1

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Regression	1	1574.437	1574.437	4.568	.0372
Residual	53	18265.508	344.632		
Total	54	19839.945			

Regression Coefficients
RDI NREM vs. Logical MP 1

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	28.271	7.788	28.271	3.630	.0006
Logical MP 1	-.219	.103	-.282	-2.137	.0372



Y = 28.271 - .219 * X; R^2 = .079

Regression Summary
RDI NREM vs. Logical MP 2

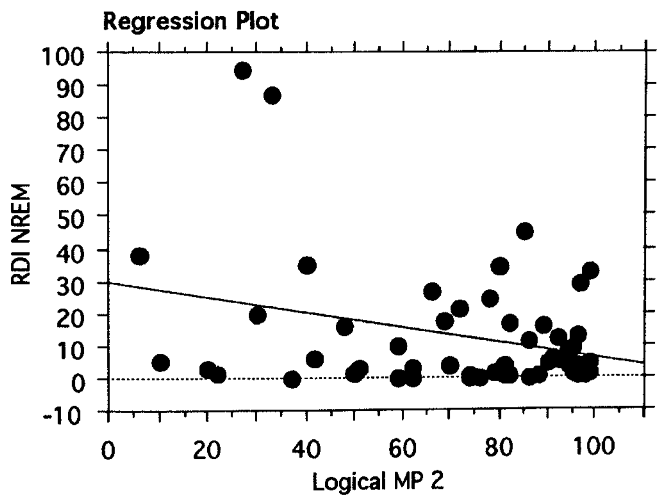
Count	55
Num. Missing	0
R	.317
R Squared	.100
Adjusted R Squared	.083
RMS Residual	18.351

ANOVA Table
RDI NREM vs. Logical MP 2

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Regression	1	1992.571	1992.571	5.917	.0184
Residual	53	17847.375	336.743		
Total	54	19839.945			

Regression Coefficients
RDI NREM vs. Logical MP 2

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	29.406	7.374	29.406	3.988	.0002
Logical MP 2	-.236	.097	-.317	-2.433	.0184



Y = 29.406 - .236 * X; R^2 = .1

Regression Summary
RDI NREM vs. PASAT

Count	52
Num. Missing	3
R	.336
R Squared	.113
Adjusted R Squared	.095
RMS Residual	18.329

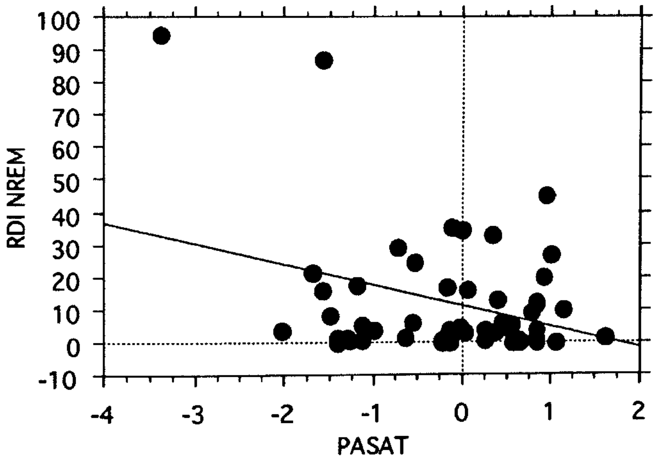
ANOVA Table
RDI NREM vs. PASAT

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Regression	1	2139.522	2139.522	6.369	.0148
Residual	50	16796.932	335.939		
Total	51	18936.454			

Regression Coefficients
RDI NREM vs. PASAT

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	11.217	2.586	11.217	4.338	<.0001
PASAT	-6.280	2.488	-.336	-2.524	.0148

Regression Plot



Y = 11.217 - 6.28 * X; R^2 = .113

The above matrices demonstrate that both immediate and delayed short term memory are adversely effected by increasing respiratory events in NREM sleep. Furthermore, there is an adverse relationship between working memory, as measured by PASAT and this sleep variable. The relationship between the NREM RDI and both logical memory I and II is best explained by the strength of the relationship between arousal and STM decrement. By multiple regression, the correlation between NREM RDI and LM1 and 2 becomes non-significant when the arousal index is forced into the equation. This is explained by the power of the correlation between the arousal index and these two cognitive outcomes. More detail with respect to these findings are presented in Chapters 3.5.1 and 3.7.

3.4.2 Cognitive outcomes versus REM RDI.

Regression Summary
RDI REM vs. Symbol digit

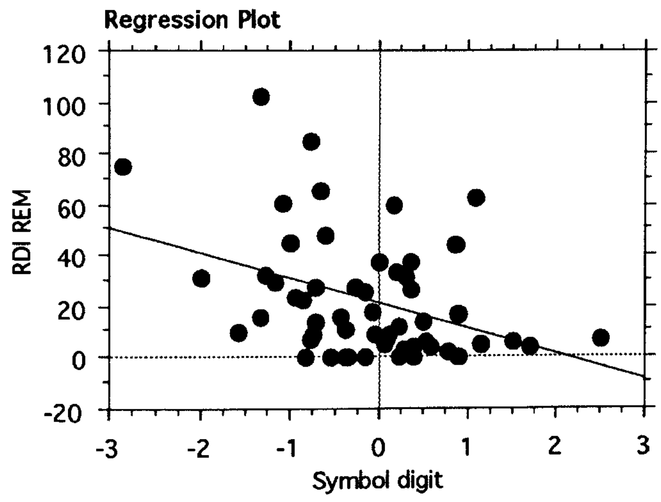
Count	55
Num. Missing	0
R	.385
R Squared	.148
Adjusted R Squared	.132
RMS Residual	22.322

ANOVA Table
RDI REM vs. Symbol digit

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Regression	1	4590.969	4590.969	9.214	.0037
Residual	53	26408.548	498.274		
Total	54	30999.517			

Regression Coefficients
RDI REM vs. Symbol digit

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	21.393	3.048	21.393	7.019	<.0001
Symbol digit	-9.828	3.238	-.385	-3.035	.0037



Y = 21.393 - 9.828 * X; R^2 = .148

This correlation demonstrates a novel relationship between increasing severity of OSA in REM sleep and a decrement in information processing speed. This finding is discussed in greater detail in Chapters 2.7 - 2.8, particularly with respect to the inability of other sleep variables to account for the strength of this observation.

3.4.3 Cognitive outcomes versus minimum saturation in NREM sleep.

Regression Summary
Min desat% NREM vs. PASAT

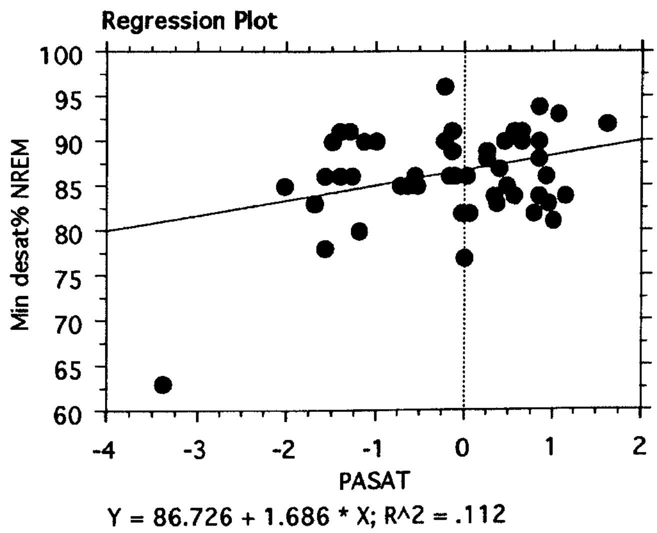
Count	52
Num. Missing	3
R	.334
R Squared	.112
Adjusted R Squared	.094
RMS Residual	4.952

ANOVA Table
Min desat% NREM vs. PASAT

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Regression	1	154.212	154.212	6.288	.0155
Residual	50	1226.307	24.526		
Total	51	1380.519			

Regression Coefficients
Min desat% NREM vs. PASAT

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	86.726	.699	86.726	124.125	<.0001
PASAT	1.686	.672	.334	2.508	.0155



The correlation above demonstrates a relationship between a decline in working memory in association with more severe hypoxia in NREM sleep. It may well account for the findings in Chapter 3.4.1 which demonstrated a similar negative correlation between PASAT and NREM RDI. Indeed, by multiple regression when PASAT is entered as the dependent variable and the NREM RDI is entered as the independent variable, if the minimum saturation in NREM is forced into the equation, the relationship between the NREM RDI and PASAT fails to reach significance. Entering the data with the minimum saturation as an independent variable and forcing the NREM RDI into the equation yields the same non-significant result as demonstrated in the tables below:

Regression Coefficients
PASAT vs. 2 Independents

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	-3.222	3.741	-3.222	-.861	.3933
RDI NREM	-.010	.011	-.193	-.911	.3668
Min desat% NREM	.037	.042	.184	.871	.3882

Regression Coefficients
PASAT vs. 2 Independents

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	-3.222	3.741	-3.222	-.861	.3933
Min desat% NREM	.037	.042	.184	.871	.3882
RDI NREM	-.010	.011	-.193	-.911	.3668

This suggests that the finding of a relationship between working memory and the magnitude of the hypoxic insult in NREM sleep is not a separate finding but relates to the magnitude of OSA in NREM generally.

3.4.4 Cognitive outcomes versus minimum saturation in REM sleep.

Regression Summary
Min desat% REM vs. Symbol digit

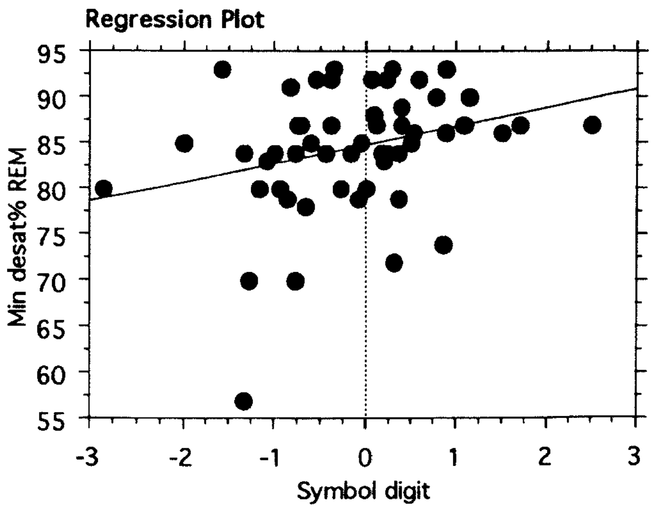
Count	54
Num. Missing	1
R	.286
R Squared	.082
Adjusted R Squared	.064
RMS Residual	6.582

ANOVA Table
Min desat% REM vs. Symbol digit

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Regression	1	199.936	199.936	4.615	.0364
Residual	52	2252.898	43.325		
Total	53	2452.833			

Regression Coefficients
Min desat% REM vs. Symbol digit

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	84.692	.907	84.692	93.400	<.0001
Symbol digit	2.051	.955	.286	2.148	.0364



Y = 84.692 + 2.051 * X; R^2 = .082

Regression Summary
Min desat% REM vs. PASAT

Count	51
Num. Missing	4
R	.308
R Squared	.095
Adjusted R Squared	.076
RMS Residual	6.624

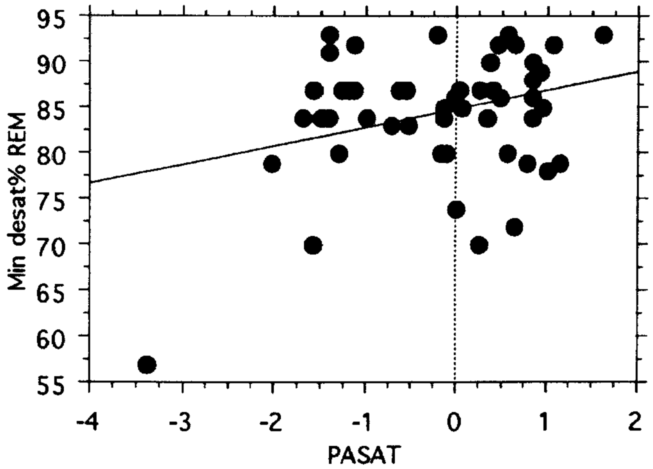
ANOVA Table
Min desat% REM vs. PASAT

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Regression	1	224.664	224.664	5.120	.0281
Residual	49	2150.316	43.884		
Total	50	2374.980			

Regression Coefficients
Min desat% REM vs. PASAT

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	84.701	.943	84.701	89.793	<.0001
PASAT	2.035	.899	.308	2.263	.0281

Regression Plot



Y = 84.701 + 2.035 * X; R^2 = .095

The finding of a relationship between the minimum saturation in REM sleep and a decline in information processing is not surprising given the strength of the simple regression analysis of the REM RDI and symbol digit. Indeed, using the same multiple regression as that discussed with respect to NREM minimum sat%, RDI and PASAT, it is evident that while the forcing of the REM minimum sat% variable diminishes the statistical power of the REM RDI versus symbol digit correlation it remains significant. Inversely forcing the REM RDI variable into the model where the REM minimum sat% is the independent variable the relationship becomes non-significant. This multiple regression is presented in the tables below:

Regression Coefficients
Symbol digit vs. 2 Independents

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	.356	2.422	.356	.147	.8838
Min desat% REM	-.002	.027	-.012	-.061	.9520
RDI REM	-.016	.008	-.398	-2.046	.0459

Regression Coefficients
Symbol digit vs. 2 Independents

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	.356	2.422	.356	.147	.8838
RDI REM	-.016	.008	-.398	-2.046	.0459
Min desat% REM	-.002	.027	-.012	-.061	.9520

Thus the finding of a statistically significant correlation between the minimum saturation in REM and the speed of information processing is largely determined by the strength of the relationship between REM RDI and symbol digit.

The demonstrated correlation between a decline in working memory, as measured by PASAT and the minimum saturation in REM sleep is of interest. Given the findings in Chapter 3.4.3 of a relationship between the minimum saturation in NREM sleep and working memory, this corroborative correlation lends force to the suggestion that a decrement in working memory is determined by the magnitude of the hypoxic injury.

3.4.5 Cognitive outcomes versus log of the time with a saturation <90% versus cognitive outcomes.

Regression Summary
Log Desat <90% vs. Logical MP 1

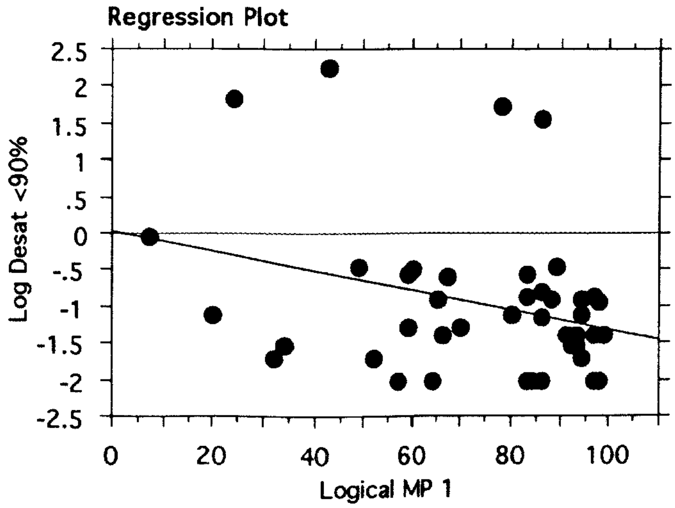
Count	43
Num. Missing	12
R	.307
R Squared	.094
Adjusted R Squared	.072
RMS Residual	1.014

ANOVA Table
Log Desat <90% vs. Logical MP 1

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Regression	1	4.381	4.381	4.261	.0454
Residual	41	42.158	1.028		
Total	42	46.539			

Regression Coefficients
Log Desat <90% vs. Logical MP 1

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	.028	.506	.028	.056	.9557
Logical MP 1	-.014	.007	-.307	-2.064	.0454



Y = .028 - .014 * X; R^2 = .094

Regression Summary
Log Desat <90% vs. Logical MP 2

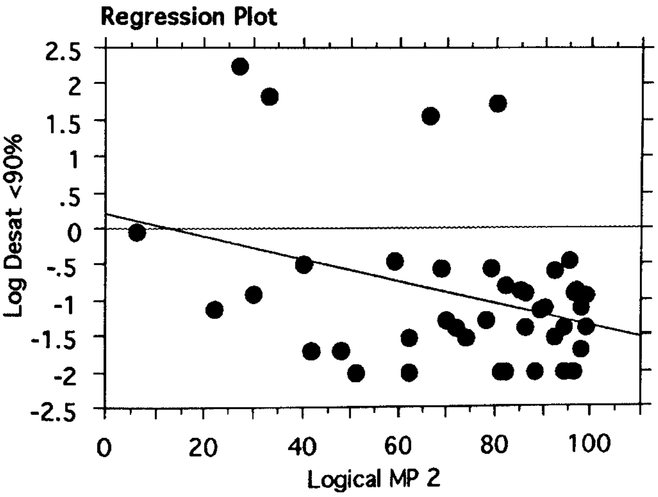
Count	43
Num. Missing	12
R	.375
R Squared	.140
Adjusted R Squared	.119
RMS Residual	.988

ANOVA Table
Log Desat <90% vs. Logical MP 2

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Regression	1	6.531	6.531	6.693	.0133
Residual	41	40.008	.976		
Total	42	46.539			

Regression Coefficients
Log Desat <90% vs. Logical MP 2

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	.222	.483	.222	.460	.6482
Logical MP 2	-.016	.006	-.375	-2.587	.0133



Y = .222 - .016 * X; R^2 = .14

Regression Summary
Log Desat <90% vs. Digitspan reverse

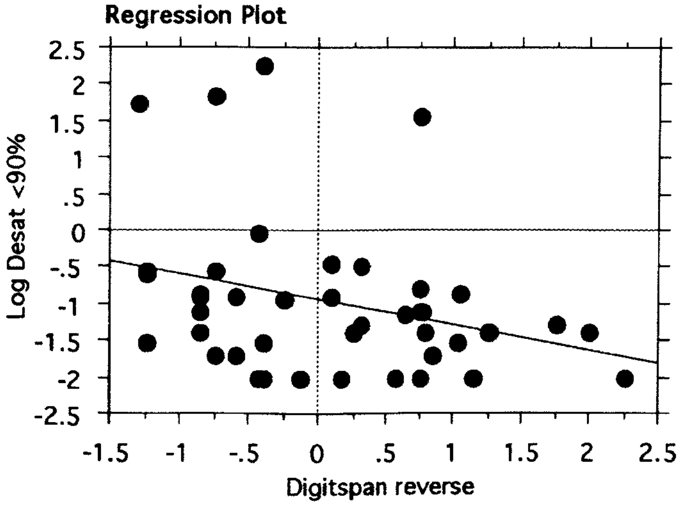
Count	43
Num. Missing	12
R	.302
R Squared	.091
Adjusted R Squared	.069
RMS Residual	1.016

ANOVA Table
Log Desat <90% vs. Digitspan reverse

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Regression	1	4.245	4.245	4.115	.0490
Residual	41	42.294	1.032		
Total	42	46.539			

Regression Coefficients
Log Desat <90% vs. Digitspan reverse

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	-.932	.156	-.932	-5.980	<.0001
Digitspan reverse	-.350	.173	-.302	-2.029	.0490



Y = -.932 - .35 * X; R^2 = .091

Regression Summary
Log Desat <90% vs. Z scores for S.C.

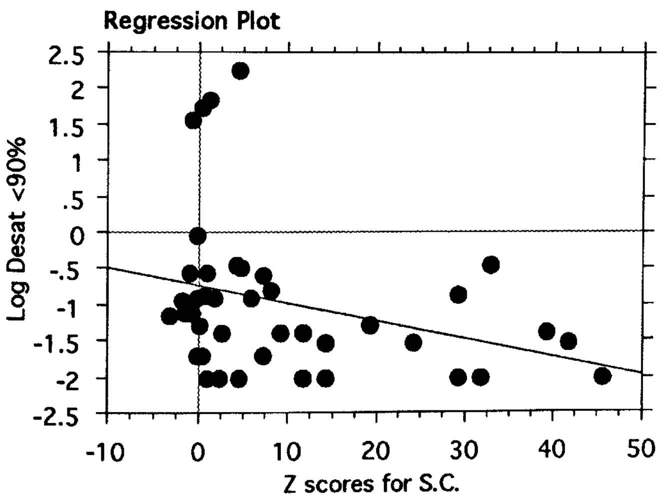
Count	43
Num. Missing	12
R	.318
R Squared	.101
Adjusted R Squared	.079
RMS Residual	1.010

ANOVA Table
Log Desat <90% vs. Z scores for S.C.

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Regression	1	4.698	4.698	4.603	.0379
Residual	41	41.841	1.021		
Total	42	46.539			

Regression Coefficients
Log Desat <90% vs. Z scores for S.C.

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	-.726	.190	-.726	-3.813	.0005
Z scores for S.C.	-.025	.012	-.318	-2.145	.0379



Y = -.726 - .025 * X; R^2 = .101

The correlation between the log of the desat% <90 (LD<90%) and a decline in both immediate and delayed short term memory is interesting, although it is difficult to interpret the independent worth of this finding given the strong internal correlation between the NREM RDI and the LD<90% (r^2 = 0.57). Furthermore there is a strong internal correlation between the arousal index and the LD<90% (r^2 = 0.40). It is therefore most likely a consequence of the relationship between the arousal index, the NREM RDI and these tests of memory function which has produced this finding. To substantiate that the magnitude of the hypoxic insult independent of either of these parameters of sleep disordered breathing was related to the decrement on short term memory alone is beyond the power of this study and is unlikely to be clinical pertinent for OSA.

The correlation between the magnitude of the hypoxic insult and the digit span reverse demonstrates further the inter-relationship between working memory and hypoxia. As a alternate type of working memory test (i.e. in contrast to PASAT) it may be more sensitive to total hypoxia than to the minimum saturation in either REM or NREM.

The finding of a relationship between the z-score for Steer Clear and the total hypoxic insult may be of some clinical significance. This is a novel finding which for the first time demonstrates a correlation between vigilance (and possibly motor vehicle accidents) and a specific measureable dimension of sleep disordered breathing. The importance of this finding and its relationship to the other measures of SDB are discussed in Chapter 3.7.

3.5 Simple regression analysis of cognitive variables versus arousals.

3.5.1 Cognitive outcomes versus total arousal index.

Regression Summary
Arousal Index vs. Logical MP 1

Count	55
Num. Missing	0
R	.365
R Squared	.133
Adjusted R Squared	.117
RMS Residual	13.650

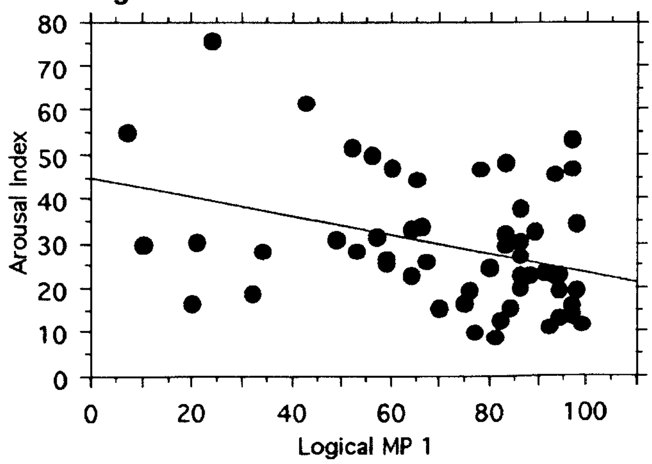
ANOVA Table
Arousal Index vs. Logical MP 1

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Regression	1	1516.979	1516.979	8.142	.0062
Residual	53	9874.909	186.319		
Total	54	11391.888			

Regression Coefficients
Arousal Index vs. Logical MP 1

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	44.791	5.726	44.791	7.822	<.0001
Logical MP 1	-.215	.075	-.365	-2.853	.0062

Regression Plot



Y = 44.791 - .215 * X; R^2 = .133

Regression Summary
Arousal Index vs. Logical MP 2

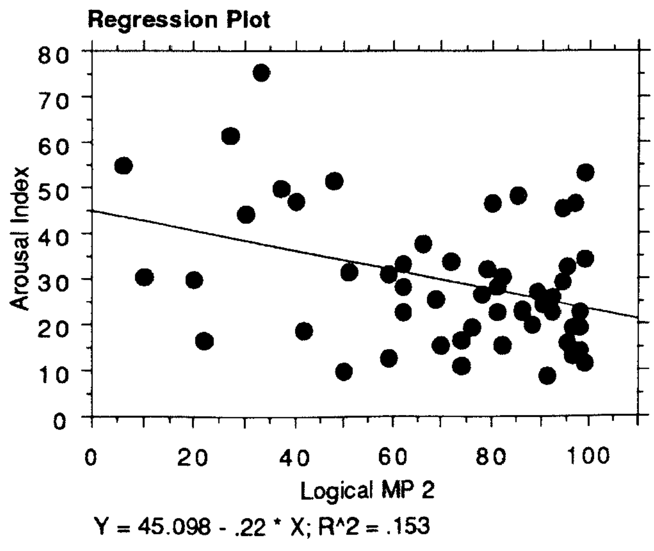
Count	55
Num. Missing	0
R	.391
R Squared	.153
Adjusted R Squared	.137
RMS Residual	13.497

ANOVA Table
Arousal Index vs. Logical MP 2

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Regression	1	1737.429	1737.429	9.538	.0032
Residual	53	9654.459	182.160		
Total	54	11391.888			

Regression Coefficients
Arousal Index vs. Logical MP 2

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	45.098	5.423	45.098	8.316	<.0001
Logical MP 2	-.220	.071	-.391	-3.088	.0032



Y = 45.098 - .22 * X; R^2 = .153

Regression Summary
Arousal Index vs. Epworth SS

Count	55
Num. Missing	0
R	.292
R Squared	.085
Adjusted R Squared	.068
RMS Residual	14.023

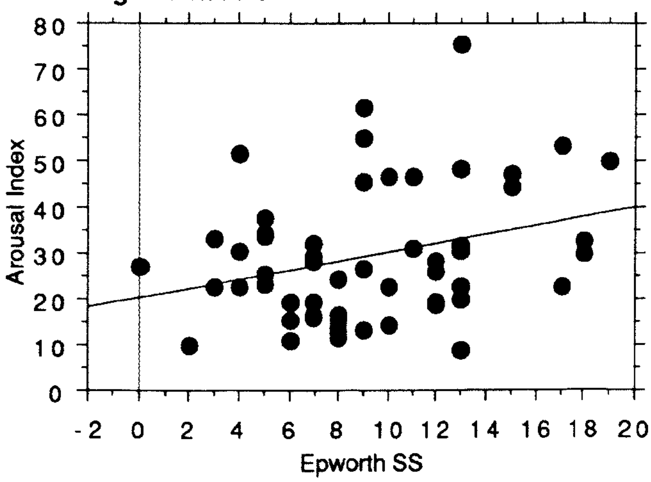
ANOVA Table
Arousal Index vs. Epworth SS

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Regression	1	969.914	969.914	4.932	.0307
Residual	53	10421.974	196.641		
Total	54	11391.888			

Regression Coefficients
Arousal Index vs. Epworth SS

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	20.365	4.453	20.365	4.573	<.0001
Epworth SS	.969	.437	.292	2.221	.0307

Regression Plot



Y = 20.365 + .969 * X; R^2 = .085

The above correlations demonstrate a negative relationship between the severity of sleep disruption and the magnitude of the decline in both immediate and delayed short term memory. This finding is discussed in greater detail in Chapters 3.7 - 3.8 and is demonstrated to be independent of the respiratory disturbance index in both NREM and REM sleep. The correlation demonstrating a relationship between the magnitude of sleep fragmentation and subjective reporting of sleepiness makes intuitive sense but has not previously been demonstrated in this manner. Examination of the regression summary demonstrates that approximately 30% of subjective somnolence can be accounted for by the degree of sleep fragmentation suggesting that other factors may be important. The lack of a demonstrable relationship between other parameters of SDB and the Epworth Sleepiness Scale (ESS) does not discount their importance to the genesis of excessive daytime sleepiness and may be the result of inherent weaknesses in the ESS and its ability to detect subtle levels of somnolence.

A separate finding from this study was an internal correlation between Steer Clear and ESS (see below).

Regression Summary
Z scores for S.C. vs. Epworth SS

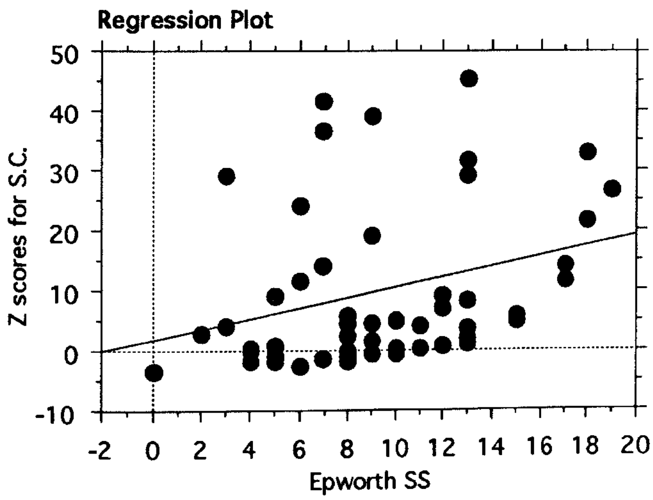
Count	55
Num. Missing	0
R	.298
R Squared	.089
Adjusted R Squared	.072
RMS Residual	12.450

ANOVA Table
Z scores for S.C. vs. Epworth SS

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Regression	1	801.609	801.609	5.172	.0270
Residual	53	8214.888	154.998		
Total	54	9016.496			

Regression Coefficients
Z scores for S.C. vs. Epworth SS

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	1.586	3.954	1.586	.401	.6899
Epworth SS	.881	.388	.298	2.274	.0270



Y = 1.586 + .881 * X; R^2 = .089

This demonstrates that subjective and objective measures of somnolence have internal validity. One possible explanation therefore would be that the arousals of SDB define the magnitude of subjective sleepiness while the magnitude of the associated hypoxia defines the decrement in objective vigilance (Steer Clear). The strong correlation between the LD <90% and the arousal index ($r^2 = 0.4$) would support this hypothesis, and suggests that a component of daytime somnolence in SDB relates to a decrement in vigilance. It is likely that both Steer Clear and ESS are insufficiently sensitive tools to be able to clearly delimit a causal association between elements of SDB and daytime sleepiness or indeed that EDS is multifactorial and no single test is likely to be predictive of sleepiness in OSA.

3.5.2 Cognitive outcomes versus modified arousal criteria.

All 55 polysomnograms were rescored utilising the modified criteria specified in Chapter 2.4.2. Each arousal sub-type was tallied using the sleep scoring software and the raw total for each type was analysed by simple linear regression against the cognitive battery. The major positive findings are presented and discussed in the following Chapters 3.5.2.1 - 3.5.2.4.

3.5.2.1 Level I arousals versus cognitive outcomes.

Regression Summary
Arousal type 1 vs. Epworth SS

Count	55
Num. Missing	0
R	.272
R Squared	.074
Adjusted R Squared	.057
RMS Residual	55.870

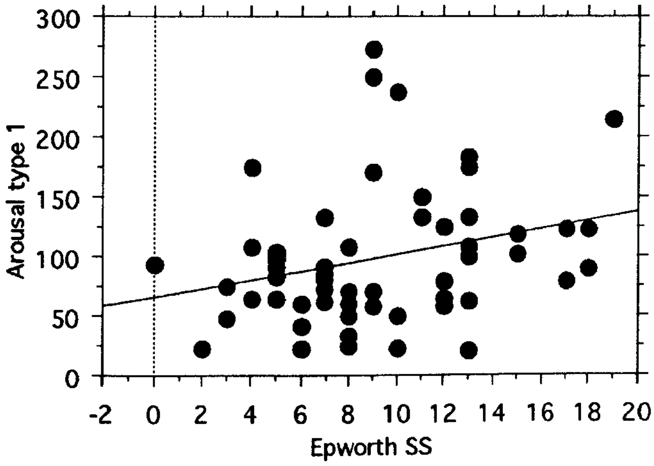
ANOVA Table
Arousal type 1 vs. Epworth SS

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Regression	1	13252.882	13252.882	4.246	.0443
Residual	53	165439.954	3121.509		
Total	54	178692.836			

Regression Coefficients
Arousal type 1 vs. Epworth SS

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	65.045	17.743	65.045	3.666	.0006
Epworth SS	3.584	1.739	.272	2.061	.0443

Regression Plot



Y = 65.045 + 3.584 * X; R^2 = .074

The correlation above demonstrates a relationship between increasing brief arousals of less than 10 seconds with increasing subjective somnolence. The relationship between the overall arousal index and sleepiness has already been demonstrated and in the absence of any other correlations between sub-types of arousals and ESS it suggests that the lesser arousals (which make up a large component of the total arousal index) are likely to be responsible for the previously demonstrated findings.

3.5.2.2 Level II arousals versus cognitive outcomes.

Regression Summary
Arousal type 2 vs. Logical MP 1

Count	55
Num. Missing	0
R	.272
R Squared	.074
Adjusted R Squared	.056
RMS Residual	25.361

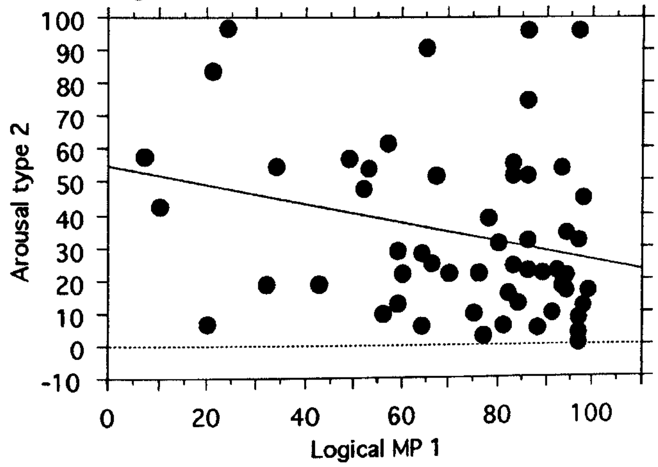
ANOVA Table
Arousal type 2 vs. Logical MP 1

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Regression	1	2719.990	2719.990	4.229	.0447
Residual	53	34088.010	643.170		
Total	54	36808.000			

Regression Coefficients
Arousal type 2 vs. Logical MP 1

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	54.717	10.639	54.717	5.143	<.0001
Logical MP 1	-.288	.140	-.272	-2.056	.0447

Regression Plot



Y = 54.717 - .288 * X; R^2 = .074

Regression Summary
Arousal type 2 vs. Logical MP 2

Count	55
Num. Missing	0
R	.228
R Squared	.052
Adjusted R Squared	.034
RMS Residual	25.658

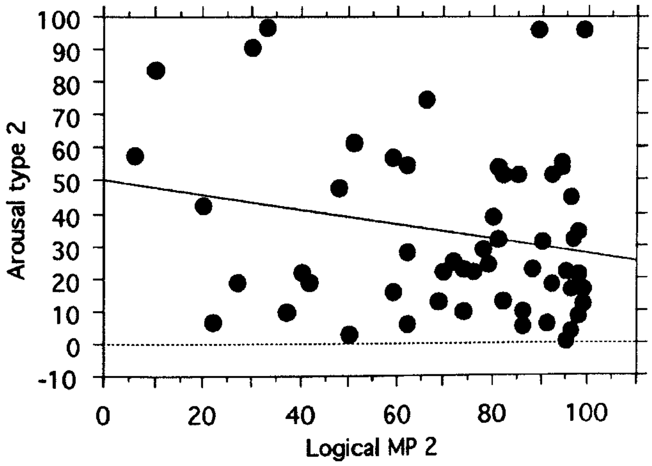
ANOVA Table
Arousal type 2 vs. Logical MP 2

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Regression	1	1917.107	1917.107	2.912	.0938
Residual	53	34890.893	658.319		
Total	54	36808.000			

Regression Coefficients
Arousal type 2 vs. Logical MP 2

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	50.574	10.310	50.574	4.905	<.0001
Logical MP 2	-.232	.136	-.228	-1.706	.0938

Regression Plot



Y = 50.574 - .232 * X; R^2 = .052

Analysis of type II arousals (i.e. those of 10-29 second duration) showed very few positive outcomes. Indeed, while a relationship to immediate short term memory was present it is substantially less statistically powerful than that demonstrated between total AI and short term memory decrement, both immediate and delayed. Furthermore, the previously significant relationship between total AI and delayed STM is not detectable at all. While the above correlation implies that arousals of longer duration may impact upon immediate STM function, the finding is overwhelmed by the previous data with respect to total AI and is likely therefore to be of research interest only and not of clinical significance.

3.5.2.3 Level III arousals versus cognitive outcomes.

Regression Summary
Arousal type 3 vs. PASAT

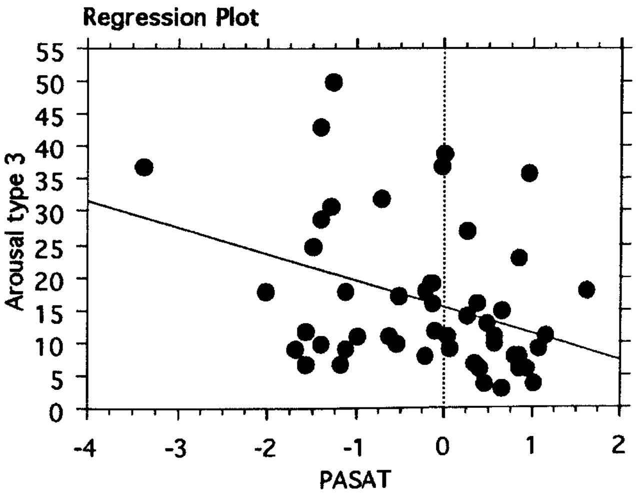
Count	52
Num. Missing	3
R	.371
R Squared	.138
Adjusted R Squared	.120
RMS Residual	10.555

ANOVA Table
Arousal type 3 vs. PASAT

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Regression	1	888.315	888.315	7.974	.0068
Residual	50	5570.358	111.407		
Total	51	6458.673			

Regression Coefficients
Arousal type 3 vs. PASAT

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	15.438	1.489	15.438	10.367	<.0001
PASAT	-4.047	1.433	-.371	-2.824	.0068



Y = 15.438 - 4.047 * X; R^2 = .138

Regression Summary
Arousal type 3 vs. Digitspan reverse

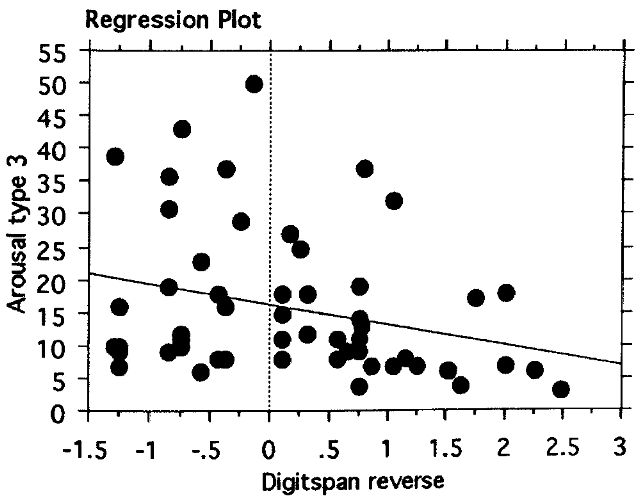
Count	55
Num. Missing	0
R	.283
R Squared	.080
Adjusted R Squared	.063
RMS Residual	10.713

ANOVA Table
Arousal type 3 vs. Digitspan reverse

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Regression	1	529.466	529.466	4.613	.0363
Residual	53	6082.716	114.768		
Total	54	6612.182			

Regression Coefficients
Arousal type 3 vs. Digitspan reverse

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	16.344	1.465	16.344	11.155	<.0001
Digitspan reverse	-3.137	1.460	-.283	-2.148	.0363



Y = 16.344 - 3.137 * X; R^2 = .08

The above relationship between type III arousals (i.e. changes in sleep stage to a lesser stage of sleep without wakefulness) and a decrement in working memory as measured by both PASAT and digit span reverse may be of considerable impoertance and somewhat unexpected. The previous analysis of total AI and these cognitive tests failed to demonstrate any relationship. However, the sub-analysis reveals a significant correlation between working memory and shifts in sleep stage. The findings above suggest that increasing sleep fragmentation when measured by shifting sleep stages may play a role in working memory decrement. This arousal scoring method would not be included in the total arousal score as it is not included in the R&K criteria, and is therefore a separate and important finding. Indeed, by multiple regression, the relationship between PASAT and type III arousals is demonstrably independent of the total AI, LD<90%, and the total RDI (see output below). These findings are still present when Vt (a general measure of intellectual ability) is entered into the regression analyses.

Regression Coefficients
Arousal type 3 vs. 3 Independents

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	23.851	11.291	23.851	2.113	.0416
Log Desat <90%	.515	1.694	.049	.304	.7628
Shipley Vt score	-.119	.190	-.098	-.624	.5366
PASAT	-3.536	1.718	-.326	-2.058	.0469

Regression Coefficients
Arousal type 3 vs. 3 Independents

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	21.281	10.624	21.281	2.003	.0508
RDI total	.017	.082	.029	.208	.8359
Shipley Vt score	-.103	.176	-.078	-.583	.5627
PASAT	-3.898	1.539	-.357	-2.532	.0147

Regression Coefficients
Arousal type 3 vs. 3 Independents

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	22.374	10.724	22.374	2.086	.0423
Arousal Index	-.037	.108	-.047	-.344	.7322
Shipley Vt score	-.099	.176	-.076	-.564	.5757
PASAT	-4.114	1.495	-.377	-2.753	.0083

3.5.2.4 Level IV arousals versus cognitive outcomes.

Regression Summary
Arousal type 4 vs. Serial digit percentiles

Count	55
Num. Missing	0
R	.343
R Squared	.117
Adjusted R Squared	.101
RMS Residual	7.975

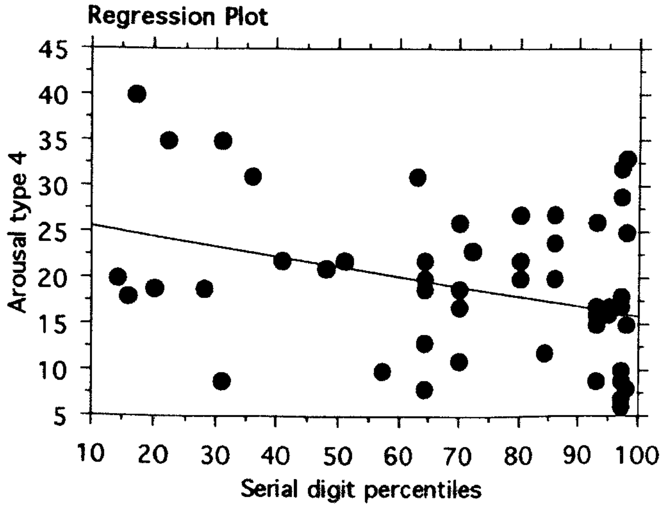
ANOVA Table
Arousal type 4 vs. Serial digit percentiles

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Regression	1	448.352	448.352	7.049	.0105
Residual	53	3371.176	63.607		
Total	54	3819.527			

Regression Coefficients
Arousal type 4 vs. Serial digit percentiles

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	26.714	3.156	26.714	8.464	<.0001
Serial digit percentiles	-.109	.041	-.343	-2.655	.0105

Regression Plot



Y = 26.714 - .109 * X; R^2 = .117

Regression Summary
Arousal type 4 vs. Digitspan reverse

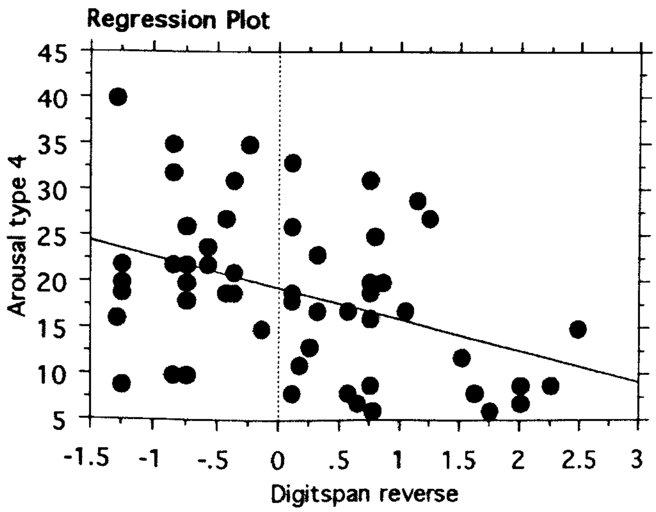
Count	55
Num. Missing	0
R	.404
R Squared	.163
Adjusted R Squared	.148
RMS Residual	7.765

ANOVA Table
Arousal type 4 vs. Digitspan reverse

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Regression	1	623.878	623.878	10.347	.0022
Residual	53	3195.649	60.295		
Total	54	3819.527			

Regression Coefficients
Arousal type 4 vs. Digitspan reverse

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	19.407	1.062	19.407	18.275	<.0001
Digitspan reverse	-3.405	1.059	-.404	-3.217	.0022



Y = 19.407 - 3.405 * X; R^2 = .163

The above correlations demonstrate a strong relationship between type IV arousals (i.e. those to full wakefulness) and digit span reverse, a measure of working memory. Indeed, as with type III arousals and PASAT the relationship between type IV arousals and digit span remains significant over and above the effects of the total AI, the total RDI or the LD<90% by multiple regression analyses (see below). Again, the effect of controlling for general intellectual ability (by entering Vt into the regression) did not alter the outcome of the analyses. The finding of a correlation between the serial digit test (supraspan learning/working memory) further corroborates the evidence of a relationship between increasing episodes of wakefulness and working memory decrement. This effect combined with the findings in the previous chapter support the hypothesis that shifting sleep states and arousal to wakefulness impair working memory despite the absence of a similar finding when the data is scored according to standard criteria.

Regression Coefficients
Arousal type 4 vs. 3 Independents

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	16.865	7.694	16.865	2.192	.0330
RDI total	.029	.056	.066	.515	.6086
Shipley Vt score	.036	.129	.037	.281	.7798
Digitspan reverse	-3.412	1.106	-.405	-3.086	.0033

Regression Coefficients
Arousal type 4 vs. 3 Independents

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	14.102	7.160	14.102	1.970	.0543
Arousal Index	.206	.070	.356	2.946	.0048
Shipley Vt score	-.014	.121	-.014	-.114	.9093
Digitspan reverse	-2.938	1.035	-.349	-2.837	.0065

Regression Coefficients
Arousal type 4 vs. 3 Independents

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	18.496	8.681	18.496	2.131	.0395
Log Desat <90%	.242	1.273	.030	.190	.8499
Shipley Vt score	.022	.146	.024	.153	.8793
Digitspan reverse	-3.261	1.549	-.348	-2.105	.0418

3.6 Simple regression analysis of cognitive variables versus somnolence measures.

Simple linear regression of all cognitive variables versus the scores for the Epworth Sleepiness Scale failed to demonstrate any statistically significant correlations. The z-scores for Steer Clear were similarly correlated against all measures of cognition. While the analysis revealed a relationship between S.C. and the Reye Complex Figure Test ($p<0.05$, $r^2 = 0.08$), this was clearly a weak relationship and possibly represents a type I error resulting from the large number of regression analyses performed. Furthermore, the finding of a decrement in untimed visuo-spatial construction and a test of vigilance is unlikely to be of clinical significance.

The findings of these analyses failed to demonstrate a relationship between the measures of somnolence and a decrement in cognition, and therefore do not support the pathway 3 hypothesis. This suggests that somnolence, at least as measured by ESS and S.C., does not contribute to the cognitive decline demonstrated elsewhere in this work.

3.7 Validation of modified arousal scoring criteria.

3.7.1 Paired t-testing.

3.7.1.1 Intra-observer scoring.

Paired t-test
Hypothesized Difference = 0

	Mean Diff.	DF	t-Value	P-Value
AI-1 score 1, AI-1 score 2	1.750	7	1.313	.2306

Paired t-test
Hypothesized Difference = 0

	Mean Diff.	DF	t-Value	P-Value
AI-2 score 1, AI-2 score 2	-2.000	7	-1.482	.1819

Paired t-test
Hypothesized Difference = 0

	Mean Diff.	DF	t-Value	P-Value
AI-3 score 1, AI-3 score 2	-.500	7	-.935	.3807

Paired t-test
Hypothesized Difference = 0

	Mean Diff.	DF	t-Value	P-Value
AI-4 score 1, AI-4 score 2	-.750	7	-1.342	.2216

Paired t-testing of all four arousal sub-types by the same primary observer demonstrates no statistically significant differences. This demonstrates that the scoring procedure was reproducible and the data derived was valid for analysis.

3.7.1.2 Inter-observer scoring.

Paired t-test
Hypothesized Difference = 0

	Mean Diff.	DF	t-Value	P-Value
Mean inter count AI-1, AI-...	.875	7	1.433	.1949

Paired t-test
Hypothesized Difference = 0

	Mean Diff.	DF	t-Value	P-Value
Mean inter count AI-2, AI-...	1.375	7	1.562	.1622

Paired t-test
Hypothesized Difference = 0

	Mean Diff.	DF	t-Value	P-Value
Mean inter count AI-3, AI-...	.500	7	1.155	.2861

Paired t-test
Hypothesized Difference = 0

	Mean Diff.	DF	t-Value	P-Value
Mean inter count AI-4, AI-...	1.125	7	2.220	.0618

Paired t-testing of the mean of both scores of the primary investigator versus the total of each of the arousal sub-types of the secondary scorer demonstrates no statistically significant differences. This demonstrates that the scoring procedure was reproducible and the data derived was valid for analysis.

3.7.2 Linear regression.

3.7.2.1 Intra-observer scoring.

Regression Summary
AI-1 score 1 vs. AI-1 score 2

Count	8
Num. Missing	0
R	.997
R Squared	.995
Adjusted R Squared	.994
RMS Residual	3.807

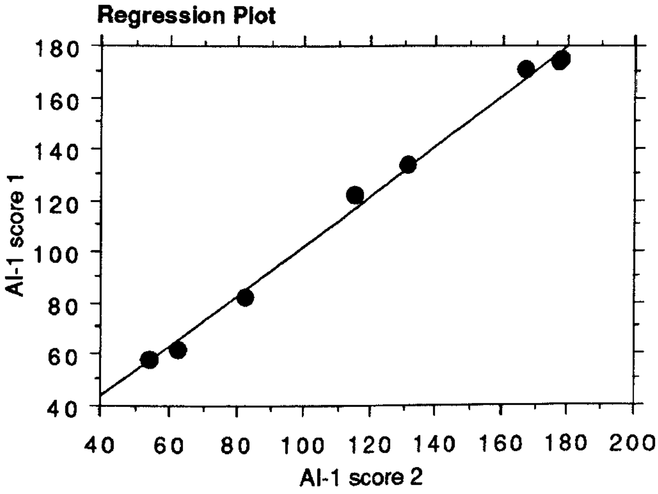
ANOVA Table
AI-1 score 1 vs. AI-1 score 2

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Regression	1	17187.025	17187.025	1185.657	<.0001
Residual	6	86.975	14.496		
Total	7	17274.000			

Regression Coefficients
AI-1 score 1 vs. AI-1 score 2

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	4.924	3.670	4.924	1.342	.2283
AI-1 score 2	.974	.028	.997	34.433	<.0001

Regression Plot



Y = 4.924 + .974 * X; R^2 = .995

Regression Summary
AI-2 score 1 vs. AI-2 score 2

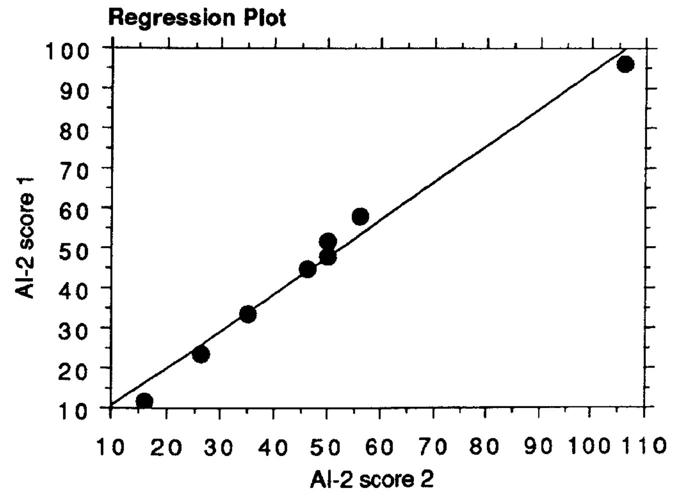
Count	8
Num. Missing	0
R	.992
R Squared	.983
Adjusted R Squared	.981
RMS Residual	3.524

ANOVA Table
AI-2 score 1 vs. AI-2 score 2

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Regression	1	4394.358	4394.358	353.825	<.0001
Residual	6	74.517	12.420		
Total	7	4468.875			

Regression Coefficients
AI-2 score 1 vs. AI-2 score 2

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	1.527	2.678	1.527	.570	.5893
AI-2 score 2	.927	.049	.992	18.810	<.0001



Y = 1.527 + .927 * X; R^2 = .983

Regression Summary
AI-3 score 1 vs. AI-3 score 2

Count	8
Num. Missing	0
R	.993
R Squared	.986
Adjusted R Squared	.983
RMS Residual	1.460

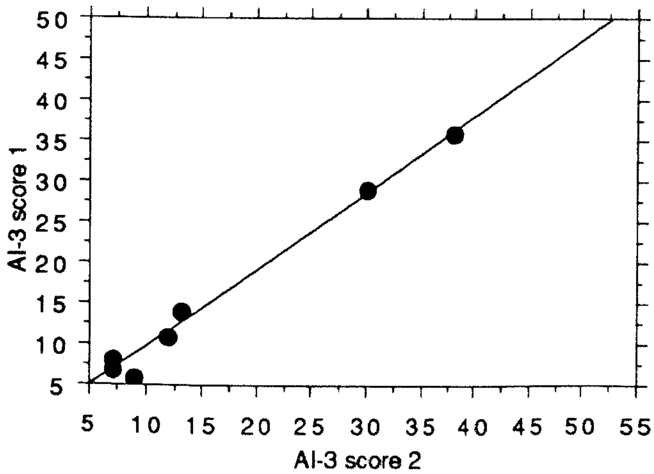
ANOVA Table
AI-3 score 1 vs. AI-3 score 2

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Regression	1	884.087	884.087	414.802	<.0001
Residual	6	12.788	2.131		
Total	7	896.875			

Regression Coefficients
AI-3 score 1 vs. AI-3 score 2

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	.374	.879	.374	.425	.6854
AI-3 score 2	.943	.046	.993	20.367	<.0001

Regression Plot



Y = .374 + .943 * X; R^2 = .986

Regression Summary
AI-4 score 1 vs. AI-4 score 2

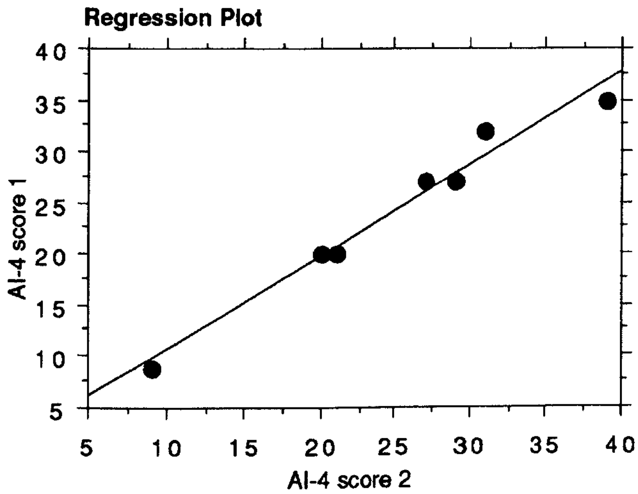
Count	8
Num. Missing	0
R	.987
R Squared	.975
Adjusted R Squared	.971
RMS Residual	1.404

ANOVA Table
AI-4 score 1 vs. AI-4 score 2

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Regression	1	463.680	463.680	235.372	<.0001
Residual	6	11.820	1.970		
Total	7	475.500			

Regression Coefficients
AI-4 score 1 vs. AI-4 score 2

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	1.691	1.521	1.691	1.112	.3087
AI-4 score 2	.900	.059	.987	15.342	<.0001



Y = 1.691 + .9 * X; R^2 = .975

The results above demonstrate a very close correlation between scores 1 and 2 for all arousal types with less than 2% variance detected. An approximate line of best fit at 45 degrees demonstrates that there is little skew of the data even with large numbers of arousals being considered.

3.7.2.2 Inter-observer scoring.

Regression Summary
AI-1 GK vs. Mean inter count AI-1

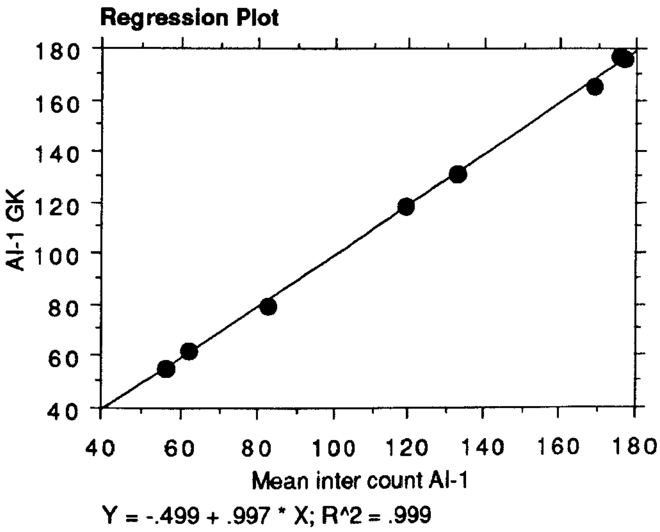
Count	8
Num. Missing	0
R	.999
R Squared	.999
Adjusted R Squared	.999
RMS Residual	1.858

ANOVA Table
AI-1 GK vs. Mean inter count AI-1

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Regression	1	17566.794	17566.794	5090.302	<.0001
Residual	6	20.706	3.451		
Total	7	17587.500			

Regression Coefficients
AI-1 GK vs. Mean inter count AI-1

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	-.499	1.822	-.499	-.274	.7933
Mean inter count AI-1	.997	.014	.999	71.346	<.0001



Regression Summary
AI-2 GK vs. Mean inter count AI-2

Count	8
Num. Missing	0
R	.997
R Squared	.995
Adjusted R Squared	.994
RMS Residual	1.865

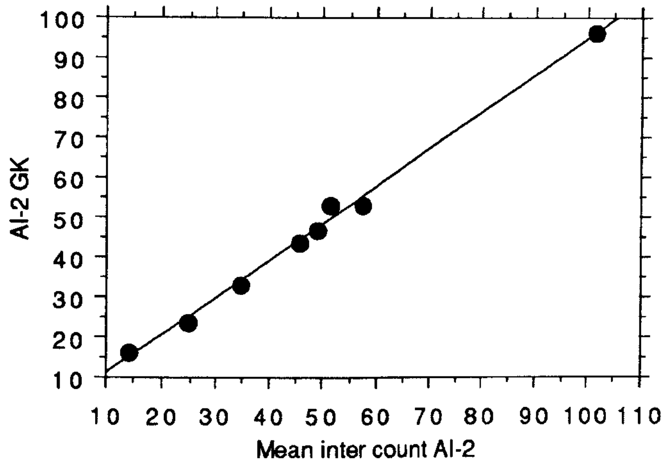
ANOVA Table
AI-2 GK vs. Mean inter count AI-2

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Regression	1	4134.640	4134.640	1189.262	<.0001
Residual	6	20.860	3.477		
Total	7	4155.500			

Regression Coefficients
AI-2 GK vs. Mean inter count AI-2

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	1.864	1.433	1.864	1.300	.2412
Mean inter count AI-2	.931	.027	.997	34.486	<.0001

Regression Plot



Y = 1.864 + .931 * X; R^2 = .995

Regression Summary
Al-3 GK vs. Mean inter count Al-3

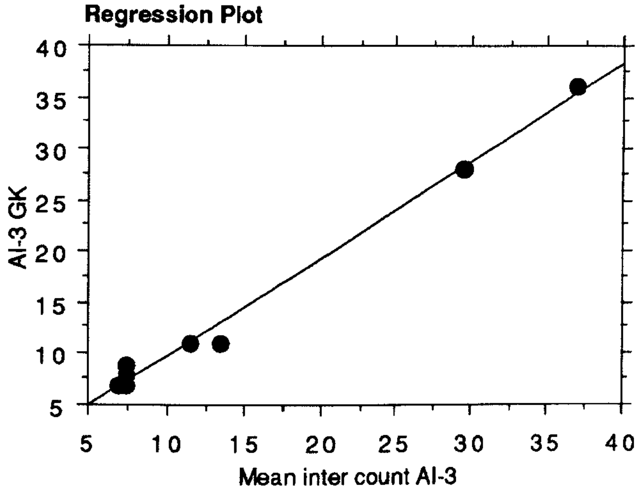
Count	8
Num. Missing	0
R	.995
R Squared	.991
Adjusted R Squared	.989
RMS Residual	1.151

ANOVA Table
Al-3 GK vs. Mean inter count Al-3

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Regression	1	845.926	845.926	638.476	<.0001
Residual	6	7.949	1.325		
Total	7	853.875			

Regression Coefficients
Al-3 GK vs. Mean inter count Al-3

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	.287	.698	.287	.411	.6951
Mean inter count Al-3	.948	.038	.995	25.268	<.0001



Y = .287 + .948 * X; R^2 = .991

Regression Summary
Al-4 GK vs. Mean inter count Al-4

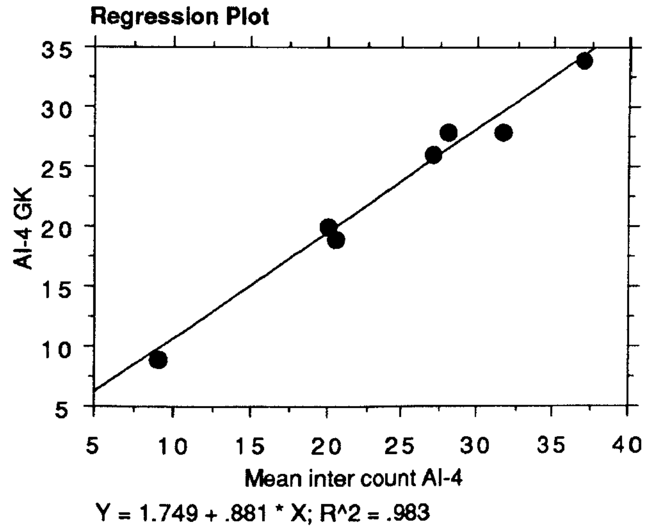
Count	8
Num. Missing	0
R	.991
R Squared	.983
Adjusted R Squared	.980
RMS Residual	1.080

ANOVA Table
Al-4 GK vs. Mean inter count Al-4

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Regression	1	402.996	402.996	345.247	<.0001
Residual	6	7.004	1.167		
Total	7	410.000			

Regression Coefficients
Al-4 GK vs. Mean inter count Al-4

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	1.749	1.206	1.749	1.451	.1971
Mean inter count Al-4	.881	.047	.991	18.581	<.0001



Y = 1.749 + .881 * X; R^2 = .983

For all analyses GK refers to the initials of the secondary scorer. Mean inter count refers to the mean total of each arousal type derived from the primary scorer. The analyses above demonstrate a good correlation for each arousal sub-type between the primary investigator and the secondary scorer. All r^2 values are >95%. Having demonstrated good concordance the outcomes for arousal scoring by modified criteria were deemed satisfactory for the subsequent analyses.

3.8 Stepwise regression analysis.

Stepwise regression was performed between each cognitive outcome and all measures of sleep disorded breathing, in order to ascertain which of the relationships were statistically independent. The following analyses comprise this step. Only statistically significant outcomes are reported. Remaining regressions are presented in Appendix 2.

Logical Memory I versus all sleep variables

Stepwise Regression Summary
Logical MP 1 vs. 7 Independents

F-to-Enter	4.000
F-to-Remove	3.996
Number of Steps	1
Variables Entered	1
Variables Forced	0
Stepwise Procedure	Forward

Variables In Model
Logical MP 1 vs. 7 Independents
Step: 0

	Coefficient	Std. Error	Std. Coeff.	F-to-Remove
Intercept	73.558	3.646	73.558	406.983

Variables Not In Model
Logical MP 1 vs. 7 Independents
Step: 0

	Partial Cor.	F-to-Enter
RDI NREM	-.383	7.063
RDI REM	-.179	1.359
Arousal Index	-.373	6.626
Min desat% NREM	.318	4.628
Min desat% REM	.227	2.221
RDI total	-.365	6.310
Log Desat <90%	-.307	4.261

Variables In Model
Logical MP 1 vs. 7 Independents
Step: 1

	Coefficient	Std. Error	Std. Coeff.	F-to-Remove
Intercept	80.458	4.285	80.458	352.619
RDI NREM	-.443	.167	-.383	7.063

Variables Not In Model
Logical MP 1 vs. 7 Independents
Step: 1

	Partial Cor.	F-to-Enter
RDI REM	.180	1.336
Arousal Index	-.110	.488
Min desat% NREM	.038	.059
Min desat% REM	-.023	.022
RDI total	.099	.396
Log Desat <90%	-.027	.030

The regression above demonstrates that the NREM RDI over and above the other sleep variables most strongly correlates with immediate short term memory decrement. Despite this, multiple regression (see Chapter 3.9) confirms that the relationship between sleep fragmentation as measured by the total arousal index and the decrement in immediate short term memory is independent of the both the total RDI and the RDI in NREM sleep when the data is corrected for general intellectual ability.

Logical Memory II versus all sleep variables

Variables In Model
Logical MP 2 vs. 7 Independents
Step: 0

	Coefficient	Std. Error	Std. Coeff.	F-to-Remove
Intercept	74.047	3.750	74.047	389.878

Variables Not In Model
Logical MP 2 vs. 7 Independents
Step: 0

	Partial Cor.	F-to-Enter
RDI NREM	-.457	10.816
RDI REM	-.141	.831
Arousal Index	-.439	9.772
Min desat% NREM	.380	6.914
Min desat% REM	.245	2.624
RDI total	-.417	8.625
Log Desat <90%	-.375	6.693

Variables In Model
Logical MP 2 vs. 7 Independents
Step: 1

	Coefficient	Std. Error	Std. Coeff.	F-to-Remove
Intercept	82.504	4.244	82.504	377.908
RDI NREM	-.543	.165	-.457	10.816

Variables Not In Model
Logical MP 2 vs. 7 Independents
Step: 1

	Partial Cor.	F-to-Enter
RDI REM	.346	5.452
Arousal Index	-.124	.627
Min desat% NREM	.048	.093
Min desat% REM	-.065	.171
RDI total	.260	2.895
Log Desat <90%	-.049	.096

Variables In Model
Logical MP 2 vs. 7 Independents
Step: 2

	Coefficient	Std. Error	Std. Coeff.	F-to-Remove
Intercept	75.595	5.000	75.595	228.553
RDI NREM	-.962	.238	-.809	16.302
RDI REM	.473	.203	.468	5.452

Variables Not In Model
Logical MP 2 vs. 7 Independents
Step: 2

	Partial Cor.	F-to-Enter
Arousal Index	-.080	.251
Min desat% NREM	.038	.058
Min desat% REM	.088	.301
RDI total	-.148	.869
Log Desat <90%	-.119	.559

The regression above demonstrates that both the NREM and REM RDI over and above the other sleep variables most strongly correlates with delayed short term memory decrement. Again, despite this, multiple regression (see Chapter 3.9) confirms that the relationship between sleep fragmentation as measured by the total arousal index and the decrement in immediate short term memory is independent of the both the total RDI and the RDI in NREM and REM sleep when the data is corrected for general intellectual ability. The most probable explanation is the very strong internal correlation between the arousal index and the RDI in either sleep state.

Symbol digit versus all sleep variables.

Stepwise Regression Summary
Symbol digit vs. 7 Independents

F-to-Enter	4.000
F-to-Remove	3.996
Number of Steps	1
Variables Entered	1
Variables Forced	0
Stepwise Procedure	Forward

Variables In Model
Symbol digit vs. 7 Independents
Step: 0

	Coefficient	Std. Error	Std. Coeff.	F-to-Remove
Intercept	-.170	.151	-.170	1.270

Variables Not In Model
Symbol digit vs. 7 Independents
Step: 0

	Partial Cor.	F-to-Enter
RDI NREM	-.262	3.015
RDI REM	-.436	9.636
Arousal Index	-.139	.813
Min desat% NREM	.184	1.436
Min desat% REM	.348	5.648
RDI total	-.316	4.563
Log Desat <90%	-.199	1.692

Variables In Model
Symbol digit vs. 7 Independents
Step: 1

	Coefficient	Std. Error	Std. Coeff.	F-to-Remove
Intercept	.334	.213	.334	2.463
RDI REM	-.018	.006	-.436	9.636

Variables Not In Model
Symbol digit vs. 7 Independents
Step: 1

	Partial Cor.	F-to-Enter
RDI NREM	.112	.511
Arousal Index	.144	.848
Min desat% NREM	-.085	.290
Min desat% REM	.076	.229
RDI total	.096	.372
Log Desat <90%	.120	.585

The regression above demonstrates the relationship between a decrement in information processing speed and the RDI in REM, and that no other variable of sleep disordered breathing had an effect over and above it. This is explored in greater depth in Chapters 3.9 - 3.10.

PASAT versus all sleep variables

Stepwise Regression Summary
PASAT vs. 7 Independents

F-to-Enter	4.000
F-to-Remove	3.996
Number of Steps	1
Variables Entered	1
Variables Forced	0
Stepwise Procedure	Forward

Variables In Model
PASAT vs. 7 Independents
Step: 0

	Coefficient	Std. Error	Std. Coeff.	F-to-Remove
Intercept	-.268	.165	-.268	2.643

Variables Not In Model
PASAT vs. 7 Independents
Step: 0

	Partial Cor.	F-to-Enter
RDI NREM	-.346	5.154
RDI REM	-.201	1.601
Arousal Index	-.244	2.415
Min desat% NREM	.333	4.749
Min desat% REM	.311	4.069
RDI total	-.330	4.632
Log Desat <90%	-.190	1.418

Variables In Model
PASAT vs. 7 Independents
Step: 1

	Coefficient	Std. Error	Std. Coeff.	F-to-Remove
Intercept	.002	.197	.002	1.116E-4
RDI NREM	-.017	.008	-.348	5.154

Variables Not In Model
PASAT vs. 7 Independents
Step: 1

	Partial Cor.	F-to-Enter
RDI REM	.100	.376
Arousal Index	.075	.207
Min desat% NREM	.110	.456
Min desat% REM	.128	.612
RDI total	.090	.301
Log Desat <90%	.111	.459

The above regression demonstrates a *significant relationship between working memory, as measured by PASAT, and the RDI in NREM sleep, and that no* other variable of sleep disordered breathing had an effect over and above it.

Digit span reverse versus all sleep variables

Stepwise Regression Summary
Digitspan reverse vs. 7 Independents

F-to-Enter	4.000
F-to-Remove	3.996
Number of Steps	1
Variables Entered	2
Variables Forced	0
Stepwise Procedure	Forward

Variables In Model
Digitspan reverse vs. 7 Independents
Step: 0

	Coefficient	Std. Error	Std. Coeff.	F-to-Remove
Intercept	.097	.138	.097	.488

Variables Not In Model
Digitspan reverse vs. 7 Independents
Step: 0

	Partial Cor.	F-to-Enter
RDI NREM	-.087	.310
RDI REM	.068	.189
Arousal Index	-.099	.407
Min desat% NREM	.208	1.854
Min desat% REM	.108	.482
RDI total	-.074	.221
Log Desat <90%	-.302	4.115

Variables In Model
Digitspan reverse vs. 7 Independents
Step: 1

	Coefficient	Std. Error	Std. Coeff.	F-to-Remove
Intercept	-.155	.182	-.155	.721
Log Desat <90%	-.260	.128	-.302	4.115

Variables Not In Model
Digitspan reverse vs. 7 Independents
Step: 1

	Partial Cor.	F-to-Enter
RDI NREM	.228	2.203
RDI REM	.361	5.989
Arousal Index	.125	.634
Min desat% NREM	-.023	.021
Min desat% REM	-.198	1.634
RDI total	.267	3.068

Variables In Model
Digitspan reverse vs. 7 Independents
Step: 2

	Coefficient	Std. Error	Std. Coeff.	F-to-Remove
Intercept	-.874	.341	-.874	6.586
RDI REM	.017	.007	.450	5.989
Log Desat <90%	-.511	.159	-.593	10.372

Variables Not In Model
Digitspan reverse vs. 7 Independents
Step: 2

	Partial Cor.	F-to-Enter
RDI NREM	.048	.089
Arousal Index	.033	.043
Min desat% NREM	.044	.075
Min desat% REM	-.067	.178
RDI total	.025	.025

The demonstrated finding of a relationship between the magnitude of the hypoxic insult and working memory is corroborated by the previously demonstrated correlation by simple linear regression. The findings of a relationship between REM RDI and digitspan reverse, when the log desat% < 90 is held constant, has no reasonable clinical explanation and was not further pursued.

Steer Clear versus all sleep variables

Stepwise Regression Summary
Z scores for S.C. vs. 7 Independents

F-to-Enter	4.000
F-to-Remove	3.996
Number of Steps	1
Variables Entered	1
Variables Forced	0
Stepwise Procedure	Forward

Variables In Model
Z scores for S.C. vs. 7 Independents
Step: 0

	Coefficient	Std. Error	Std. Coeff.	F-to-Remove
Intercept	9.507	2.023	9.507	22.087

Variables Not In Model
Z scores for S.C. vs. 7 Independents
Step: 0

	Partial Cor.	F-to-Enter
RDI NREM	-.145	.879
RDI REM	-.179	1.354
Arousal Index	-.018	.013
Min desat% NREM	.227	2.229
Min desat% REM	.277	3.405
RDI total	-.162	1.108
Log Desat <90%	-.318	4.603

Variables In Model
Z scores for S.C. vs. 7 Independents
Step: 1

	Coefficient	Std. Error	Std. Coeff.	F-to-Remove
Intercept	5.642	2.649	5.642	4.538
Log Desat <90%	-4.004	1.866	-.318	4.603

Variables Not In Model
Z scores for S.C. vs. 7 Independents
Step: 1

	Partial Cor.	F-to-Enter
RDI NREM	.155	.982
RDI REM	.036	.053
Arousal Index	.250	2.663
Min desat% NREM	-.011	.005
Min desat% REM	.057	.129
RDI total	.141	.816

The finding of a significant relationship between Steer Clear and the magnitude of the hypoxic insult over and above other sleep variables is a novel finding and will be discussed in greater detail in Chapter 3.8.

Epworth Sleepiness Scale versus all sleep variables

Stepwise Regression Summary
Epworth SS vs. 7 Independents

F-to-Enter	4.000
F-to-Remove	3.996
Number of Steps	0
Variables Entered	0
Variables Forced	0
Stepwise Procedure	Forward

Variables In Model
Epworth SS vs. 7 Independents
Step: 0

	Coefficient	Std. Error	Std. Coeff.	F-to-Remove
Intercept	9.279	.621	9.279	223.209

Variables Not In Model
Epworth SS vs. 7 Independents
Step: 0

	Partial Cor.	F-to-Enter
RDI NREM	.225	2.192
RDI REM	.237	2.439
Arousal Index	.264	3.078
Min desat% NREM	-.010	.004
Min desat% REM	-.133	.737
RDI total	.228	2.240
Log Desat <90%	.104	.449

Although simple linear regression demonstrates a correlation between the ESS and the total arousal index, forward stepwise regression does not demonstrate this finding to be significant over and above the other variables of sleep disordered breathing. The simple regression supports hypothesis pathway 4, but suggests that this pathway is not independent of the hypoxic pathway.

SUMMARY OF FINDINGS:

Thus the major findings of the stepwise forward regression analyses can be summarised as follows:

Logical memory I and II	NREM RDI
Symbol digit	REM RDI
PASAT	NREM RDI
Digit span reverse	Log of time with a saturation <90%
Steer Clear	Log of time with a saturation <90%

3.9 Multiple regression analysis.

Based upon the findings of the simple linear and stepwise regressions, further analysis of the data set was performed in an effort to examine whether the relationships demonstrated were likely to prove of clinical significance and indeed whether the various overlapping components of sleep disordered breathing could be separated and used to determine specific cognitive decrements.

3.9.1 Logical Memory I and II versus arousal index, NREM and total RDI.

To test the strength of the relationship between sleep fragmentation (arousals) and the measured decline in short term memory, multiple regression was performed using the arousal index as the independent variable. General intellectual ability was controlled by forcing Vt (t-score of the Shipley Living Institute of Living Scale) into the model. This did not diminish the significance of the relationship ($p = 0.0013$ for LM1, $p = 0.0007$ for LM2). Having already determined that the total RDI, the NREM RDI and the arousal index were strongly correlated (for total RDI $p < 0.0001$, $r2 = 0.56$, for NREM RDI $p < 0.0001$ $r2 = 0.60$), the total RDI and the NREM RDI were separately forced into the previous model. While the p value, as expected due to the strong internal correlations, were diminished, they remained statistically significant (see below)

Regression Coefficients
Logical MP 1 vs. 3 Independents

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	57.957	22.340	57.957	2.594	.0123
Shipley Vt score	.580	.375	.200	1.546	.1283
RDI NREM	.060	.260	.047	.232	.8177
Arousal Index	-.714	.345	-.421	-2.068	.0437

Regression Coefficients
Logical MP 1 vs. 3 Independents

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	57.598	22.266	57.598	2.587	.0126
Shipley Vt score	.599	.377	.207	1.589	.1182
RDI total	.117	.252	.091	.464	.6447
Arousal Index	-.769	.333	-.454	-2.310	.0250

Regression Coefficients
Logical MP 2 vs. 3 Independents

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	63.451	23.251	63.451	2.729	.0087
Shipley Vt score	.499	.391	.165	1.277	.2076
RDI NREM	.001	.271	4.388E-4	.002	.9983
Arousal Index	-.722	.359	-.408	-2.009	.0499

Regression Coefficients
Logical MP 2 vs. 3 Independents

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	63.391	23.161	63.391	2.737	.0085
Shipley Vt score	.531	.392	.175	1.356	.1810
RDI total	.122	.262	.091	.465	.6440
Arousal Index	-.844	.346	-.476	-2.436	.0184

Thus, increasing sleep fragmentation independent of the total respiratory disturbance index and the NREM RDI correlates with a decrements in both immediate and delayed short term memory, despite the fact that many of the arousals may have been respiratory in origin. This finding supports hypothesis pathway 1.

Given the above finding, in addition to the stepwise analysis suggesting a significant relationship between the NREM RDI and Logical memory I and II, the same multiple regression model was applied to the correlation between memory deficits and the NREM RDI. Again, the Vt did not significantly alter the outcome. However, when the arousal index is forced into the equation where

NREM RDI is the independant variable, the p value fails to reach statistical levels for both Logical memory I and II (see below).

Regression Coefficients
Logical MP 1 vs. 3 Independents

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	57.957	22.340	57.957	2.594	.0123
Shipley Vt score	.580	.375	.200	1.546	.1283
Arousal Index	-.714	.345	-.421	-2.068	.0437
RDI NREM	.060	.260	.047	.232	.8177

Regression Coefficients
Logical MP 2 vs. 3 Independents

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	63.451	23.251	63.451	2.729	.0087
Shipley Vt score	.499	.391	.165	1.277	.2076
Arousal Index	-.722	.359	-.408	-2.009	.0499
RDI NREM	.001	.271	4.388E-4	.002	.9983

Thus, it appears that much of the of the relationship between short term memory deficit and the NREM RDI is related to the strength of the relationship between arousals and memory decrement rather than being an important separate finding.

3.9.2 Symbol digit versus REM RDI.

Using the same technique described above, symbol digit was regressed against the REM RDI using the Vt as a forced variable to control for general intellectual ability. Subsequently, the total AI was separately entered to examine their contribution to the relationship.

Regression Coefficients
Symbol digit vs. 3 Independents

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	-.639	.855	-.639	-.748	.4581
Shipley Vt score	.011	.014	.096	.740	.4625
Arousal Index	.009	.010	.147	.951	.3462
RDI REM	-.018	.006	-.458	-2.965	.0046

Thus the relationship between a decline in information processing speed and the increasing REM RDI is independent of the overall degree of sleep fragmentation. Given that the total RDI also correlated with a decline in the normed score of the Symbol Digit test, the same analytical method was applied to this relationship.

Regression Coefficients
Symbol digit vs. 3 Independents

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	-.965	.873	-.965	-1.106	.2740
Shipley Vt score	.011	.015	.104	.777	.4405
Arousal Index	.016	.013	.246	1.217	.2292
RDI total	-.023	.010	-.469	-2.330	.0238

Again, there is no demonstrable effect when controlling for general intellect by Vt. Forcing the arousal index into this model does not alter the relationship (prior to forcing AI $p = 0.04$, post forcing AI $p= 0.02$) although the strength of the correlation is not as powerful as that of REM RDI and SD. Of note, when performing the same regression forcing the NREM RDI as an independent variable, no correlation with a decline in information processing was demonstrated. Thus it seems that a decline in information processing speed correlates with increasing REM apnoea. The relationship is independent of NREM apnoea and the impact of sleep fragmentation. The fact that the total RDI is similarly (but more weakly) correlated is most likely due to the strong internal correlation between total RDI and REM RDI ($p = 0.0005$, $r^2 = 0.73$).

To ensure that the effect was not related to the total amount of REM sleep, further analyses were performed. The total number of respiratory events in REM was calculated by multiplying the REM RDI by the total REM sleep time. The same multiple regression analyses were performed using the total REM arousals as the independent variable and symbol digit as the dependent variable. The total RDI, arousal index and log desat <90% were then forced into the equation and Vt entered to control for general intellectual ability (see below).

Regression Coefficients
Symbol digit vs. 3 Independents

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	-.388	.866	-.388	-.449	.6555
Shipley Vt score	.008	.014	.075	.575	.5681
Arousal Index	.002	.009	.038	.280	.7810
Total REM resp. events	-.017	.006	-.420	-3.050	.0036

Regression Coefficients
Symbol digit vs. 3 Independents

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	-.377	.863	-.377	-.437	.6641
Shipley Vt score	.009	.014	.084	.652	.5174
RDI total	-.002	.008	-.045	-.272	.7868
Total REM resp. events	-.015	.007	-.377	-2.254	.0285

Regression Coefficients
Symbol digit vs. 3 Independents

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	-.366	.951	-.366	-.385	.7021
Shipley Vt score	.013	.015	.121	.857	.3968
Log Desat <90%	.084	.155	.090	.542	.5907
Total REM resp. events	-.021	.007	-.508	-3.049	.0041

The analyses demonstrate that respiratory events, of sufficient magnitude to contribute to the RDI in REM, correlate with a decline in speed of information processing independent of the total amount of REM sleep present or other variables of sleep disordered breathing. This supports hypothesis pathway 2, and demonstrates that specific components of sleep disordered breathing may contribute to a decrement in performance in certain areas of the test battery.

3.9.3 PASAT and Digit span reverse versus NREM RDI and log of the desat% < 90.

To further examine the relationship between PASAT and Digitspan (reverse), as measures of working memory, and the variables NREM RDI and log desat%<90, both were entered as dependent variables into multiple regression matrices. Forcing Vt into the equations did not alter the p values significantly. However, when AI was forced into each equation the relationships became statistically non significant, despite the fact that AI has no correlation with either PASAT (p = 0.12) or Digitspan reverse (p = 0.28) by simple linear regression.

Regression Coefficients
PASAT vs. 3 Independents

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	-.344	1.001	-.344	-.343	.7328
Shipley Vt score	.004	.017	.032	.234	.8162
Arousal Index	.007	.015	.092	.431	.6685
RDI NREM	-.022	.011	-.405	-1.902	.0631

Regression Coefficients
Digitspan reverse vs. 3 Independents

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	-1.921	.896	-1.921	-2.146	.0382
Shipley Vt score	.027	.015	.278	1.859	.0706
Arousal Index	.005	.012	.077	.401	.6908
Log Desat <90%	-.276	.166	-.320	-1.665	.1039

Thus, the relationship between the magnitude of the hypoxic insult, the magnitude of NREM sleep apnoea and the decline in working memory should be considered non-significant when the additional insult of sleep fragmentation is taken into account. This suggests that not all components of hypothesis pathway 2 are independent of the other variables of sleep disordered breathing, namely the input of pathway 1 (sleep fragmentation and cognitive impairment).

3.9.4 Steer Clear versus the log of the desat% < 90.

In order to further understand this intriguing and novel finding and having determined that AI confounded the relationship between the log desat%<90 and Digitspan reverse, the same statistical principles were applied to the relationship between Steer Clear (SC) and this measure of hypoxia, given the correlation by simple regression. Having entered the normed scores for Steer Clear as the dependent variable, log desat%<90 was entered independently . Vt was forced into the equation to control for general intellectual ability. The total arousal index was then separately entered. The regression analyses demonstrated that, in fact, the relationship was strengthened when Vt was entered to control for general intellect (p = 0.014). Furthermore, when AI was forced into the matrix, the statistical significance became clearer (see below).

Regression Coefficients
Z scores for S.C. vs. 3 Independents

	Coefficient	Std. Error	Std. Coeff.	t-Value	P-Value
Intercept	26.488	11.766	26.488	2.251	.0301
Shipley Vt score	-.627	.194	-.436	-3.241	.0024
Arousal Index	.385	.156	.427	2.471	.0179
Log Desat <90%	-8.014	2.180	-.636	-3.677	.0007

Thus, the relationship between vigilance and the magnitude of the hypoxic insult, unlike that of working memory, remains significant. Indeed, contrary to the finding of a diminished correlation, the magnitude of sleep fragmentation appears to augment the existing relationship between vigilance decrement and magnitude of the hypoxic insult. Again, this in part supports hypothesis pathway 2, and suggests that some performance decrements within the test battery are significantly related to separate components of sleep disordered breathing.

3.10 Secondary analysis of outcomes and the derivation of odds ratios.

The major findings of the study and those deemed to be of most clinical significance were the relationship between REM RDI and speed of information processing and that of sleep fragmentation and short term memory impairment. Given that adequate numbers of subjects had been studied and the correlations were sufficiently significant, secondary analysis of these two outcomes was undertaken. Each neuropsychological test was normed and then divided into quartiles of performance. The intersection of the specificity and sensitivity curves was determined by inspection against the respiratory parameter of interest (i.e. REM RDI for Digit Symbol and arousal index for LM1 and LM2). The odds ratio at each quartile of cognitive performance versus the level of sleep disturbance was then calculated using the standard formula and are presented in the tables below.

RDI REM versus the performance of Symbol Digit

Performance Percentile	REM RDI	odds ratio	C.I.
25th %tile	37	2.7	0.7 - 10.38
50th %tile	14	3.2	1.04 - 9.65
75th %tile	5	3.6	0.96 - 13.8

AI versus the performance of Logical memory passages I

Performance Percentile	Arousal Index	odds ratio	C.I.
25th %tile	37	2.35	0.57 - 3.67
50th %tile	26	1.94	0.66 - 5.67
75th %tile	19	2.3	0.60 - 8.74

AI versus the performance of Logical memory passages II

Performance Percentile	Arousal Index	odds ratio	C.I.
25th %tile	34	5	1.3 - 18.84
50th %tile	26	4.1	1.12 - 15.25
75th %tile	19	2.6	0.69 - 10.54

Thus, a predicted level of cognitive decrement (and the odds ratio) were able to be calculated for a given level of sleep fragmentation and REM related sleep apnoea. The clinical importance of these findings is discussed in the following Chapter 4.