SYSTEMATIC INTER-INDIVIDUAL VARIABILITY IN SLEEP VARIABLES: COMPARING FINDINGS FROM THE GENERAL POPULATION TO TWIN STUDY RESULTS

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INTRODUCTION

Limited information has been published regarding systematic inter-individual differences in PSG-assessed sleep variables for the general population.[1] However, a handful of papers have more elaborately investigated systematic differences among and within twin pairs.[2-9] From results published by Linkowski and colleagues[4,5] it is possible to derive the variances among and within monozygotic (MZ) and dizygotic (DZ) twin pairs. In this investigation, we worked out equations to calculate these numbers, and used them to compare the variability among twin pairs to our findings for inter-individual variability in non-twin individuals published elsewhere in this volume.[1]

METHODS

Two studies by Linkowski et al.[4,5] provided sufficiently detailed information to allow us to calculate variability among and within twin pairs. These studies involved male MZ and DZ twin pairs selected to be healthy regular sleepers. The first study[4] involved 14 MZ and 12 DZ twin pairs (ages 16–35), 11 of which were non-cohabiting. The second study[5] involved 11 MZ and 15 DZ non-cohabiting twin pairs (ages 20–36), 11 of which were also part of the first study. In the two studies, subjects went to bed around 23:00 and were allowed to wake up spontaneously in the morning. PSG recordings were taken during 3 consecutive nights. The records were visually scored according to conventional criteria.[10] The following variables were reported (in minutes): total sleep time (TST), duration of sleep stage 2 (S2), duration of sleep stages 3 and 4 (SWS), duration of REM sleep, latency to sleep stages 1 and 2 (SL1 and SL2, respectively), and REM latency (REML) as measured from stage 1 sleep onset.

Linkowski and colleagues reported their results in terms of mean square (M) values. From the M values it is possible to derive the among-twin-pair variances σ^2_{AMZ} and σ^2_{ADZ} (for MZ and DZ twin pairs, respectively). As put forward by Christian et al.,[11] the variances among MZ and DZ twin pairs, respectively, are given by:

$$\sigma^2_{AMZ} = \frac{M_{AMZ} - M_{WMZ}}{2}, \quad (1)$$

$$\sigma^2_{ADZ} = \frac{M_{ADZ} - M_{WDZ}}{2}. \quad (2)$$

The M values reported by Linkowski et al.[4,5] may be expressed in terms of additive (σ_a^2), dominant (σ_d^2) and epistatic (σ_i^2) genetic variance; environmental variance (σ_e^2); covariance between genetic and environmental effects (σ_{ge}); covariance among environmental effects between pairs of twins (C); and a function of epistatic variance within DZ twin pairs$\left(f\right)$[11]:

$$M_{AMZ} = 2\sigma_{aMZ}^2 + 2\sigma_{iMZ}^2 + 2\sigma_{dMZ}^2 + \sigma_{eMZ}^2 + 4\sigma_{geMZ} + C_{MZ}\,, \quad (3)$$

$$M_{WMZ} = \sigma_{eMZ}^2 - C_{MZ}\,, \quad (4)$$

$$M_{ADZ} = 1.5\sigma_{aDZ}^2 + \left(1+f\right)\sigma_{iDZ}^2 + 1.25\sigma_{dDZ}^2 + \sigma_{eDZ}^2 + 4\sigma_{geDZ} + C_{DZ}\,, \quad (5)$$

$$M_{WDZ} = 0.5\sigma_{aDZ}^2 + \left(1-f\right)\sigma_{iDZ}^2 + 0.75\sigma_{dDZ}^2 + \sigma_{eDZ}^2 - C_{DZ}\,. \quad (6)$$

Substituting Eqs. (3) and (4) into Eq. (1), and Eqs. (5) and (6) into Eq. (2), yields:

$$\sigma_{AMZ}^2 = \sigma_{aMZ}^2 + \sigma_{iMZ}^2 + \sigma_{dMZ}^2 + 2\sigma_{geMZ} + C_{MZ}\,, \quad (7)$$

$$\sigma_{ADZ}^2 = 0.5\sigma_{aDZ}^2 + f\sigma_{iDZ}^2 + 0.25\sigma_{dDZ}^2 + 2\sigma_{geDZ} + C_{DZ}\,. \quad (8)$$

The total variance among and within twin pairs is the sum of the genetic and environmental variances and interactions[12]:

$$\sigma_{MZ}^2 = \sigma_{aMZ}^2 + \sigma_{iMZ}^2 + \sigma_{dMZ}^2 + \sigma_{eMZ}^2 + 2\sigma_{geMZ}\,, \quad (9)$$

$$\sigma_{DZ}^2 = \sigma_{aDZ}^2 + \sigma_{iDZ}^2 + \sigma_{dDZ}^2 + \sigma_{eDZ}^2 + 2\sigma_{geDZ}\,. \quad (10)$$

Furthermore, the total variance for MZ and DZ twin pairs can be partitioned as the sum of the among- and within-twin-pair variance components, as follows:

$$\sigma_{MZ}^2 = \sigma_{AMZ}^2 + \sigma_{WMZ}^2\,, \quad (11)$$

$$\sigma_{DZ}^2 = \sigma_{ADZ}^2 + \sigma_{WDZ}^2\,. \quad (12)$$

Substitutions of Eqs. (4), (7) and (9) into Eq. (11), and Eqs. (6), (8) and (10) into Eq. (12), lead to:

$$\sigma_{WMZ}^2 = M_{WMZ}\,, \quad (13)$$

$$\sigma_{WDZ}^2 = M_{WDZ}\,. \quad (14)$$

Use of Eqs. (1), (2), (13) and (14) allows for the calculation of ICC values,[13] defined as:

$$ICC_{MZ} = \frac{\sigma_{AMZ}^2}{\sigma_{AMZ}^2 + \sigma_{WMZ}^2}\,, \quad (15)$$

$$ICC_{DZ} = \frac{\sigma_{ADZ}^2}{\sigma_{ADZ}^2 + \sigma_{WDZ}^2}\,. \quad (16)$$

The ICC ranges from 0 to 1, and quantifies the stability of inter-individual differences.

RESULTS AND DISCUSSION

Tables 1 and 2 display the results obtained for the among- and within-twin-pair variances as well as the ICC values, for the sleep variables considered in the two Linkowski papers.[4,5] As expected, the within-twin-pair variances were consistently smaller for the MZ twin pairs than for the DZ twin pairs (whereas this was not always the case for the among-twin-pair variances). High ICC values were found in the MZ twins for S2 and SWS. The much lower ICC values for these same sleep variables in the DZ twins (see Tables 1 and 2) indicate that S2 and SWS demonstrated considerable genetic effects.[9]

For comparison, Table 3 shows results for repeated baseline sleep recordings in 21 non-twin adults (ages 22–40; 11 females), as observed by Tucker and Van Dongen.[1] From a genetic and statistical perspective, measuring sleep repeatedly over time within the same individual is equivalent to measuring sleep in each member of a MZ twin pair. The interpretation of the between- and within-subject variances in Table 3 is therefore equivalent to the among- and within-twin-pair variances, respectively, for the MZ twins in Tables 1 and 2. A comparison of the non-twin between-subject variances (Table 3) with the among-MZ-twin-pair variances (Tables 1 and 2) showed that the variability among non-twins[1] was consistently greater than the variability among MZ twin pairs,[4,5] although the differences were striking only for SL1, SL2 and REML. The latter may have to do with the fact that the subjects examined by Tucker and Van Dongen[1] went to bed at 22:00, which may have caused the wake maintenance zone[14] to interfere with sleep onset in some individuals. Alternatively, gender effects may have been involved, as only the Tucker and Van Dongen report included females.[1]

The variability within non-twins[1] (Table 3) was also consistently greater than the variability within MZ twin pairs[4,5] (Tables 1 and 2), but this result by itself is difficult to interpret because of methodological differences between the studies (e.g., subjects stayed in bed longer in the study reported by Tucker and Van Dongen[1]). Yet, a comparison of the ICC values indicates that the stability of inter-individual differences was greater for the MZ twin pairs[4,5] than for the non-twin individuals,[1] except for REM and REML. Although the reason for such dissimilarity is unclear, it suggests that laboratory observations of considerable systematic inter-individual variability in sleep variables for the general population may still underestimate the true underlying trait variability.

Table 1. Among- and within-twin-pair variances and ICC values[a,b] for Linkowski et al., 1989.[4]

	Monozygotic			*Dizygotic*		
	σ^2_{AMZ}	σ^2_{WMZ}	ICC_{MZ}	σ^2_{ADZ}	σ^2_{WDZ}	ICC_{DZ}
TST	821	264	0.76	548	497	0.52
S2	646	107	0.86	403	510	0.44
SWS	1177	49	0.96	783	324	0.71
SL2	49	39	0.55	113	53	0.68

[a]Results for REM and SL1 not reported.[4]
[b]REML not defined in a comparable manner[4] and therefore not considered here.

Table 2. Among- and within-twin-pair variances and ICC values[c] for Linkowski et al., 1991.[5]

	Monozygotic			*Dizygotic*		
	σ^2_{AMZ}	σ^2_{WMZ}	ICC_{MZ}	σ^2_{ADZ}	σ^2_{WDZ}	ICC_{DZ}
TST	823	220	0.79	2342	312	0.88
S2	842	56	0.94	481	460	0.51
SWS	1195	53	0.96	647	274	0.70
REM	43	118	0.26	142	203	0.41
SL1	27	13	0.68	32	51	0.38
REML	57	185	0.23	212	338	0.38

[c]Results for SL2 not reported.[5]

CONCLUSIONS

Through Eqs. (1) and (2),[11] and Eqs. (13) through (16) worked out by us, it is possible for the first time to compare findings of inter-individual differences in the general population to results from twin studies published previously. Our comparison of variability among MZ twin pairs, derived from published data[4,5] as described here, with variability among non-twin adults sampled by us from the general population,[1] provided convergent evidence for the existence of systematic inter-individual differences in sleep parameters. The twin study data,[4,5] as reworked and evaluated in this paper, suggested that inter-individual differences may be even more stable than the results from our laboratory observations[1] would seem to indicate.

As pointed out by Linkowski,[9] genetic factors appear to underlie some of the systematic differences among twin pairs. Our ability to show such systematic differences among non-twin individuals also[1] may open the door to genetic studies of sleep in the general population.

Table 3. Between- and within-subject variances[d] and ICC values for baseline sleep in Tucker and Van Dongen, this volume.[1]

	σ^2_{BS}	σ^2_{WS}	*ICC*
TST	2042	1972	0.51
S2	1448	1077	0.57
SWS	1634	399	0.80
REM	255	505	0.34
SL1	1686	1173	0.59
SL2	1502	1450	0.51
REML	882	935	0.49

[d]Units were converted into minutes, instead of hours as originally reported.[1]

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