Recall performance in acutely depressed patients and plasma cortisol

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Introduction
It has been conjectured that memory impairment in depression mainly reflects problems with effortful processing and minimally with automatic processing [13]. Memory impairment in depression has also been associated with cortisol hypersecretion [5,18 - 21], although the relation is still unclear [9]. A total recall score in free recall of a list of words has been mostly used as a measure of performance. The serial position curve, in which various parts are independently sensitive to qualitative different forms of memory performances [3], has never been used. Furthermore, the relationship between memory impairment in depression and cortisol hypersecretion has been mainly assessed after oral dexamethasone intake [7]. Dexamethasone intake, however, does not rule out cortisol hypersecretion [17] and may furthermore influence memory performance [22]. To search for specific relationships of unsuppressed plasma cortisol and recall performance according to the serial position curve of words, we used the same method employed in an earlier study [4].

Material and Methods
Subjects
We compared 15 recently admitted patients (8 males, 7 females, aged 60.3 ± 14.2 years, with 8.4 ± 3.2 years of education) with a major depressive syndrome as per DSM-III-R criteria [1] and 6 in-stay patients (4 males, 2 females, aged 56.1 ± 14.8 years, with 8.1 ± 1.6 years of education) with DSM-III-R schizophrenia, ill for more than 25 years, and 9 normal controls (3 males, 6 females, aged 59.4 ± 16.3 , with 8.0 ± 1.5 years of education) matched for age, sex and years of education, were compared. Both patient groups were taking neuroleptics and benzodiazepines. The depressed group was additionally taking antidepressants and lithium. The groups did not differ significantly in their usage of lithium, neuroleptics and benzodiazepines.

The severity of depression was assessed by means of a Dutch version of the Mont-
gy-Asberg Depression Rating Scale (MADRS) [12]. The scores ranged from 1 to 35 with a mean of 22.67 ± 9.93.

**Cortisol measures**

Plasma cortisol measurements were done at 9, 12 and 16 hours. Cortisol was determined by high-performance liquid chromatography (HPLC) with ultraviolet (UV) detection. In short the assay was as follows. Within 1 hour after venipuncture plasma was separated and frozen at -20°C until used. After thawing, prednisolone was added as internal standard. Plasma was alkalinized and cortisol was extracted into dichloromethane; after evaporation of the organic solvent the sample was dissolved in the eluent and injected on a HPLC cartridge CP® SPHER Si. The eluent consisted of a mixture of 335 ml dichloromethane, 150 ml dichloromethane saturated with water, 6ml tetrahydrofuran, 12 ml methanol and 0.25 ml acetic acid. Cortisol was detected at 254 nm. The lower limit of detection is 10 nmol/l plasma; within-day and day-to-day variation are 4.6 % and 8.7 % respectively. In our laboratory the reference values used are 0.16 - 0.50 μmol/l at 09 h and 0.08 - 0.30 μmol/l at 16 h.

**Memory assessment**

The test, a method employed in an earlier study [4], consisted of five trials and immediate free-recall of a 6-word list, a 9-word list and the 6- and 9-word list on aggregate. Words were read at a speed of 1½ s/word. Serial position curves of the accumulated recall over five trials of the 6-, 9- and 15-word list were drawn. To test for alterations of the primacy part and recency part, the first four positions of 6-, 9- and 15-word list and the last four positions of the 9- and 15-word list were grouped and summed up over the five consecutive trials. Memory assessment occurred on the day of venipuncture.
Data Analysis

Analysis of variance was performed on the primacy and recency parts. To ascertain possible effects of psychotropic medication on cognitive function, performance on the primacy and recency parts was reanalyzed by means of Analysis of Covariance (ANCOVA). Pearson correlation coefficient was computed between the recall performance per positions of the lists and plasma cortisol values. In order to take into account the effects of multiple hypothesis testing, p was set at 0.016.

Results

Serial position curves are depicted in Figures 1 a,b and c. One-way ANOVA’s of the primacy and recency parts showed significant (p < 0.016) group differences between the depressed patients and normals controls on the primacy part and between the depressed patients and schizophrenic patients on the recency part of the 9-word list. ANCOVA’s performed, to account for psychotropic effects on the primacy and recency parts showed significant (p <0.016) group differences between all three groups on the primacy parts of the 6-, 9- and 15-words list, but no difference on the recency parts.

Eight depressed patients (5 males, 3 females, aged 56.1 ± 14.8 years, with 8.1 ± 1.6 years of education) agreed to plasma cortisol measurements. Consent could not be accounted for by the severity of their depression. Nor could hypercortisolism of 9.00 or 16.00 hours of six patients account for any differential effects on memory performance. As can be read from Table 1 significant positive (p <0.016) correlations with plasma cortisol were found in depressed patients for position 4 of the 6-word list, positions 4 and 5 of the 9-word list and 3 and 8 of the 15-word list, while a significant negative correlation was found for position 9 of the 9-word list.

Though no single significant correlation at p <0.016 was found for the schizophrenic patients, all correlations at 9.00 hours were negative, of which four with a p <0.05.
Fig 1 a,b,c. The serial position curves of multi-trial free recall of the 6,9 and 15 words.
Discussion

Impaired recall performance on the primacy part of the three lists for the depressed and schizophrenic patients is in agreement with the results of single-trial free recall with depressed elderly [10] and schizophrenic patients [15]. Our results also show that the usage of psychotropic medication may obscure existing differences and suggest nonexisting ones. The primacy part of the serial position curve has been associated with effortful processing [14] and the recency part with automatic processing [8]. Our data confirm that depressed and schizophrenic patients have problems with effortful processing [11,13].

We further found positive correlations between plasma cortisol secretion and positions of the primacy part and a negative correlation between plasma cortisol secretion and the recency part. These results suggest that in depression cortisol secretion is positively associated with effortful processing, and negatively associated with automatic processing.

Although no significant correlations were found in the schizophrenic group, the predominantly negative correlations suggest that cortisol secretion is negatively associated with memory processing and warrant further study.

As unsuppressed plasma cortisol is subject to considerable diurnal and interindividual variation from day to day, we reanalyzed our data correlating the area under the curve (AUC) of the plasma cortisol values with the serial positions. Again positive correlations (p=0.004) were found for position 5 of the 6-word list, positions 3 (p=0.047), 4 (p=0.024) and 8 (p=0.016) of the 15-word list and a negative correlation for position 9 (p= 0.034) of the 9-word list in the depressed group. No significant correlations were found in the schizophrenic group.

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References


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<sup>a</sup> The other positions had no significant correlations

NS= p > 0.05