A computational approach to the anamnestic collection in neuro-ophthalmology: the Analytic Anamnestic Protocol

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Abstract
In neuro-ophthalmology the clinical management cannot help but start with an accurate anamnestic evaluation. In this case signs and symptoms depend not only on the severity of the alleged disease, but also on the degree of impairment that affects the two functional domains the visual system is made of: namely, the visuomotor and the visuosensory domains (VMD and VSD). The Analytic Anamnestic Protocol (AAP) is a set of questions devised to measure the effect clinical features affecting relatives may have on the actual clinical condition of the patient, as well as to mathematically analyze past and actual symptoms reported by the subject. Each answer is assigned a score that expresses the amount of visuomotor (M) and visuosensory (S) impairment. At the end of the protocol the final M- and S-scores are computed as the sum of M and S at each response. This way the expected proportion between visuomotor and visuosensory alteration in the patient can be computed. The questionnaire has been administered to 200 normal subjects, 98 patients suffering from cerebral lesion, 75 dyslexics and 24 patients with Down syndrome. In the pathological groups M- and S-scores were higher compared to the normal sample. In particular S- and M-score in dyslexics revealed a main visuosensorial impairment (median S-score: 9 (IR=13), median M-score: 2 (IR=3). In the other two samples the VMD and VSD involvement turned out to be roughly the same. ROC curves, sensitivity and specificity demonstrated the AAP to be a valid alternative to the current medical history collection, having the advantage to quantify and characterize predisposing factors towards the disease. In conclusion the Analytic protocol proves to be a valid alternative to the current medical history collection, having the advantage to quantify and characterize predisposing factors towards the disease. In this context the AAP provides the physician with preliminary information that, supplemented by diagnostic instrumental data and by the clinical examination, is expected to increase the diagnostic accuracy.

Introduction
In neuro-ophthalmology the assessment of a (suspect) patient cannot help but start with accurate anamnasis. In this case signs and symptoms are related not only to the severity of the alleged disease, but also to the degree of impairment that affects the motor and the sensory domains of the visual system (visuomotor and visuosensory domain, VMD and VSD).
In order to improve the first phase of the clinical management it would be therefore desirable to make the anamnestic phase more informative by performing a mathematical analysis of the gathered data. Turning the diagnostic findings into a numerical outcome has been proposed in the past so as to improve the accuracy in predicting the onset of a disease based on clinical as well as biochemical variables. Macchia et al, for example, devised a diagnostic score for the metabolic syndrome aimed at predicting diabetes by appropriately weighting the single metabolic parameters [1]. Tosetto et al proposed a prediction score (DASH) to estimate the risk of disease recurrence in subjects with
unprovoked venous thromboembolism [2]. Similarly, the Framingham Risk Score estimates the 10-year risk of coronary heart disease [3] and Menekse et al developed a score model to predict mortality in patients with perforated peptic ulcer [4]. Score systems have been introduced not only to estimate the risk of pathological occurrence, but also to improve the diagnostic confidence: it is the case of the diagnostic score of Kruis, which weights symptoms like pain and flatulence, laboratory findings like white blood cells count and erithrosedimentation rate, and anamnestic data like history of blood in stool to increase the probability to correctly diagnose irritable bowel syndrome [5].

In the ophthalmological field the STAAR scoring system or the East London Glaucoma Prediction Score (ELGS) have been devised to judge the risk of developing glaucoma [6, 7].

Still, anamnestic data are particularly important when dealing with poor collaborative patients, like infant and children, for whom clinical tests can be demanding and often biased, therefore scarcely informative. Yet, for its own qualitative nature anamnestic data are not suited to be processed numerically, so that at best they actually have only guidance value.

In order to extrapolate more rigorously preliminary (i.e. pre-diagnostic) indications on the presence of a neuro-ophthalmological condition in adults and children and on its relative degree of visuomotor / visuosensorial impairment, a specific tool, the Analytic Anamnestic Protocol (AAP), has been developed. The AAP aims at analyzing the clinical elements reported in close relatives (parents or brother/sisters) and the symptoms reported by the patients or by their parents by assigning each answer a score; this way, the AAP aims at quantifying the likelihood of a pathological condition in the subject under examination and, in case, it seeks to predict the relative amount of visuomotor or visuoperceptive impairment.

Methods

In its original version, AAP is a set of 27 questions organized into four anamnestic phases: familiar, general, remote past and recent past specialist medical history. Each answer is assigned a specific visuomotor or visuoperceptive weight by means of a score. The value of the score depends on the strength of the supposed relation between the reported datum and VMD or VSD. For example, reporting ambliopia in a parent of the subject or occasional visual blurring in the subject him/herself is given a sensory score (S=2 and 8, respectively), whereas referring occasional diplopia is attributed a motor score (M=7). The final M- and S-scores are computed as the sum of the collected S- and M-values for each question. This way, final S and M outcome reflects the expected sensorial and visuomotor involvement.

By plotting M- and S-scores as x- and y- coordinates on a Cartesian graph the degree and type of visuoperceptive impairment as expected in the patient can be represented.

Participants

Two hundred normal subjects (Norm group, age 1-80 years, median 12 years, interquartile range, IR: 35 years), 98 patients suffering from cerebral lesion (Cl group, age 1-73 years, median 5 years, IR: 7.75 years), 75 dyslexics (Dysl group, age 7-17 years, median 9 years, IR: 11 years), and 24 subjects with Down syndrome (Down group, age 1-21 years, median 6 years, IR: 8 years) were administered the AAP. The Cl group encompassed children affected by cerebral palsy, other neurological disorders as well as adult subjects with ischemic lesions involving to a different extent the brain hemispheres. In the Dysl group subjects were diagnosed as suffering from developmental dyslexia by a neuropsychiatry service. The Down group was recruited from a center specialized in physical and mental disability. In all cases patients were referred to the Neuro-ophthalmology Center for a neuro-ophthalmological evaluation. Norm group was made of subjects who underwent a routinary ophthalmological check-up. The study has been examined and approved by the ethics committee and has therefore been performed in accordance with the ethical standards laid down in the 1964 declaration of Helsinki. All applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed.
Results

Figure 1 shows the distribution of the M-/S- scores related to each patient belonging to the four groups. In the normal sample, the few positive anamnestic elements are localized about the bisecting line, within a limited region on the lower left side of the graph. We will refer to this x-y boundary as the paraphysiological region. We have stated the paraphysiological region to extend till to the 95° percentile of the distribution of the normative scores, that is $S=5, M=2$.

This disposition means than normal subjects, as expected, show scarce anamnestic positivity, involving, when it occurs, the VMD and VSD to a roughly equal degree. Median S-score was 2 (IR=3), median M-score was 0 (IR=1).

In the dyslexic group scores are located below the bisecting line and spread toward the right, crossing over beyond the paraphysiological region. Such a pattern reflects elements predisposing to a pathological condition and suggests main impairment in the visuosensory domain. As a matter of fact, the median VSD-related score is 9 (IR=13), whereas the median VMD-related score is 2 (IR=3).

Finally, in the CI and Down sample the scores are located between the bisecting line, most of them scattered well beyond the paraphysiological region. The median VSD- and VMD-related score are: CI= 8 (IR=11.7), and 10 (IR=17), and: Down= 7 (IR=10) and 5 (IR=9), respectively.

The anamnestic relevance on the pathological condition can be deduced by comparing the overall median scores computed as the sum $S+M$ in each pathological sample with those of the normative sample. The total score is 3 in the normative sample, 11 in the dyslexic group, 18 in the cerebral lesions.
and 12.5 in patients suffering from Down syndrome. Compared to the control group, the total score in the Cl, Dysl and Down were statistically significant (Kruskal-Wallis [KW=446.72], p < .0001; Dunn: norm vs dysl, norm vs cl, norm vs Down: p< .001: figure 2, left panel). The proportion of alteration in the VSD compared to the MSD can be inferred by computing the partial scores S and M in the pathological samples (figure 2, right panel).

Figure 3. AAP-related Receiving Operator Characteristic curves. A: overall pathological sample; b: Dysl, c: Cl; d: Down.

After administering the AAP, the expected impairment in the VSD turned out to be greater in the three pathological samples compared to the normative group (Kruskal-Wallis [KW=261.32]: p<.0001; Dunn: Norm vs Dysl, Norm vs Cl, Norm vs Down: p< .001). In turn, no significant difference was found in the VS abnormality relative to Cl, Dysl and Down (Dunn: p>.05). The same occurs for VM (Kruskal-Wallis [KW=240.13]: p< .0001; Dunn: Norm vs Dysl, Norm vs Cl, Norm vs Down: p< .001). In addition, in this case the score was lower in Dysl than in Cl and Down (Dunn: p< 0.001).

Sensibility and specificity of the AAP is represented as ROC curves in figure 3. Considering as a whole the three pathological samples, AAP sensibility and specificity is 76.3% and 92.5%, respectively. Relative to the dyslexic sample, it is 92.9% and 86.6%, relative to the group with cerebral lesions it is 98.7% e 95.5%; finally, relative to the Down group it is 85.3 e 95.5%.

Conclusion

In conclusion the AAP is a mathematical approach aimed at providing a suggestion on the clinical problem before the diagnostic phase takes place. In this respect the AAP is more effective compared to the conventional collection of information about the patient's medical history, since it is able to quantify and characterize the predisposing factors as found in relatives and the actual visual problems as reported by the subject in his/her everyday life.

An additional advantage is that it is suitable not only to the specialized doctors but also as a screening pre-test for optometrists or general practitioners.

The main weakness of the method is its euristic criterion for the assignment of the score. In addition, further in-depth analysis is necessary to test the AAP sensitivity and specificity in respect to a wider range of (neuro)ophthalmological diseases.

However, according to this preliminary investigation the AAP seems able to provide, after being complemented by the diagnostic data, a more comprehensive overview of the clinical situation. Finally, it might help reduce the amount of prescribed instrumental examinations, allowing to control the healthcare expenditure.
References


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Topics

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