Study is predicated upon our previous reported work in this subject over the last 15 years.2-4 It is, in our view, essential to be consistent in the use of the tested and validated instruments. For example, the Northwick Park Activities of Daily Living (ADL) Index2 and the Frenchay Index3 are both well-established tools, as are the psychological and behavioral instruments that we also utilize. Our study is not a controlled trial; it is an observational study with meticulous control of data collection procedures, and the nature of this basically anthropological study is such that it needs to use robust and reliable instruments over a lengthy period of time.

We are disappointed in the response to our short communication by Shah and Cooper. Obviously, neither the occasion nor the context of this report lends itself to the details of a full formal communication. We did not, for example, have an opportunity to discuss in any detail the fundamental importance of the concepts of ADL competence and ADL performance, a subject on which we have recently written and shall shortly be publishing.

Most of the criticisms are not relevant to an abbreviated report of a paper given at an invited symposium and could be just as incorrectly applied to most of the other contributions to this excellent symposium.

Finally, we are not only "content to use the less-discriminative 3-point scale" in our ADL Index, but feel that its tested and published accuracy and undoubted functional relevance clearly vindicate its application and continued use in this important area of study.

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References


Responses of Rat Basilar Artery to Acetylcholine and Platelet Products In Vivo

To the Editor:

Faraci et al1 reported vasoactive responses of rat basilar artery to platelet products in vivo. They found more potent responses for basilar artery than for pial arterioles, a difference which they suggest could be related to the vessel size. Based on their extravascular topical applications of several agents, they suggested that extravascular, as well as intravascular, platelet aggregation byproducts might play a role in such conditions as subarachnoid hemorrhage or intra-arterial thromboembolism.2

We recently described rupture of the arterial wall in two cases of leptomeningeal thromboembolism.3 We suggested that, at the level of the occluded arterial segment, which has a healthy and relatively thick media, the embolism could induce direct intimal injury. The resulting stimulation of the smooth muscle cells would provoke an arterial spasm, leading to rupture of the wall.

We also are not forgetting that the clot, which releases vasoconstrictor agents, could play a role in causing spasm. The experimental results of Faraci et al1 help explain more completely a fact already pathologically illustrated.3 Such vasoactive responses may have important clinical implications, as in cases of embolic migration, hemorrhagic infarct, subarachnoid hemorrhage, or even nonhypertensive intracerebral hemorrhage,4-6 a fact nevertheless as yet unrecognized.7

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References


The following is in response:
To the Editor:

We appreciate the interest and comments of Drs. De Smet and Brucher regarding our recent paper.1 We agree that the findings may have clinical implications. One might speculate, based on the findings, that extravascular aggregation of platelets following subarachnoid hemorrhage, and perhaps intravascular aggregation in atherosclerotic arteries, may produce important effects on cerebral blood vessels. Vascular responses to individual platelet products suggest that the net effect of these products would result in much greater constriction of large cerebral arteries than of arterioles in the microcirculation.

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Reference


Effect of Elevated Norepinephrine Levels on Electrocardiographic Changes in Subarachnoid Hemorrhage

To the Editor:

In their article, Grad and colleagues1 purport to show that prolonged QT, intervals or abnormal U waves are not correlated with increased plasma norepinephrine levels observed after sub-
arachnoid hemorrhage. This is surprising because human and animal studies have established that these changes are directly associated with catecholamine infusion or increased cardiac sympathetic nerve activity.\(^5\)\(^6\) Indeed, ablation of the left inferior cervical ganglion is a recognized therapy for malignant idiopathic QT\(_r\) prolongation (Romano-Ward syndrome).\(^5\) There are several explanations for these discrepancies, and we would urge the authors to consider these before concluding, as they did in their article, that increased sympathetic activity is unrelated to the electrocardiographic (ECG) changes. First, it is likely that the ECG changes take some time to develop in the face of increased sympathoadrenal activity. Once initiated, increased catecholamine concentrations after stroke (and, in particular, after subarachnoid hemorrhage) are associated with a specific form of cardiac damage termed myocytolysis.\(^7\)\(^8\) Similar cardiac changes are also observed following exogenous administration of catecholamines to normal individuals or in phaeochromocytoma.\(^9\) It is probable that the ECG changes are representative of this structural damage, which may persist for some weeks or months.\(^10\)\(^\text{-}^13\)

Populations of subarachnoid hemorrhage patients may therefore be heterogeneous, comprising those whose plasma catecholamine levels have normalized but whose hearts were earlier exposed to high levels and who now have ECG changes on a persisting structural basis. In addition, there will be some patients earlier in the course of their catecholamine careers whose levels are rising and who are developing the ECG and structural changes, and others whose catecholamine levels remain elevated. These are the patients whose ECG changes correlated with elevated plasma norepinephrine levels. Some evidence for such heterogeneity comes from this study. At 24 hours, 20 patients showed raised plasma norepinephrine levels, whereas at 3 days, 26 patients demonstrated this abnormality. At its simplest, six additional patients must have crossed from the normal to the elevated catecholamine group. In all likelihood, there was greater interchange in both directions between the groups. The best way of dealing with this issue is to correlate ECG changes with plasma norepinephrine levels on an individual patient basis and to sample more frequently, say, every 6 hours. The QT\(_r\) interval is often difficult to measure owing to errors in placement of the isoelectric line and background noise. Therefore, a more valid method of comparison would exist between the mean values and standard deviations of the groups, not merely how many were abnormal in each group. Quite possibly, the increased plasma norepinephrine group had longer QT\(_r\) values than those whose plasma norepinephrine levels were not elevated. Likewise, an assessment of change in the QT\(_r\) values for individual patients over time, correlated with plasma norepinephrine levels, would be of greater value.

Some of the patients in this study may exhibit QT\(_r\) interval prolongation for reasons other than alteration of plasma catecholamine levels. These include medications such as anticoagulants. We are given no information on this point. QT\(_r\) interval and U wave abnormalities may also accompany changes in plasma epinephrine.\(^3\) These levels are elevated in subarachnoid hemorrhage as they are after ischemic stroke.\(^14\)\(^15\) It is surprising that there is no mention of this catecholamine in this study. Therefore, before concluding that the ECG changes are unrelated to catecholamine levels, a correlation with plasma epinephrine should be performed.

A further explanation for these discrepancies may be that plasma norepinephrine levels do not reflect cardiac sympathetic nerve activity. Thus, activity within the cardiac nerves may be inadequate to produce a sufficient catecholamine spillover to affect the general plasma level. The source of the elevated plasma norepinephrine may therefore be adrenal rather than neural. In the absence of information about plasma epinephrine, this hypothesis cannot be examined.

We respectfully submit that further attention be given to this important matter before a conclusion is drawn that flies in the face of considerable accumulated evidence.

**References**


The following is in response:

To the Editor:

In their critical appraisal of our article,\(^1\) Drs. Oppenheimer and Hachinski raise several relevant points well worth discussing, and we are grateful for this opportunity to clarify them as far as possible.

We agree that ECG changes observed in our subarachnoid hemorrhage (SAH) patients might have resulted from cardiac myocytolysis; however, since most patients scored 1 or 2 on the Hunt-Hess scale, the myocardial pathological changes must have been slight and easily reversible.

The correlation of ECG changes with plasma norepinephrine (NE) levels on an individual patient basis revealed that the same 20 patients who had elevated NE levels on admission retained them 3 and 7 days after the bleed. Three days after SAH, they were joined by six patients who had had normal NE levels on admission; of these, the NE level increase was considerable in four and slight in two. Increased NE levels were observed again on day 7 after SAH in the former four patients and returned to normal in the latter two patients. Thus, these results do not support any great
Effect of elevated norepinephrine levels on electrocardiographic changes in subarachnoid hemorrhage.
S Oppenheimer and V Hachinski

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